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UNITED STATES NAVY

MEDICAL NEWS LETTER

Editor - Captain F. W. Farrar, MC, USN

Vol. 16 Friday, 14 July 1950 No. 1

SPECIAL NOTICE

PHYSICIANS, DENTISTS, AND NURSES NEEDED FOR ACTIVE DUTY

The recently authorized increase in the over-all man power strength of the Navy requires the services of additional Medical Department personnel to serve in the continental United States and overseas.

Because of the acute shortage of physicians, dentists, and nurses now on active duty and required to meet the present-day obligations, the Surgeon General of the Navy is making an appeal to members of the inactive Naval Reserve, and to civilian physicians, dentists, and nurses not now affiliated with the Naval Reserve.

Members of the inactive Naval Reserve are asked to volunteer immediately for extended active duty. Medical and dental officers are desired in the ranks of commander and below, and nurses in the ranks of lieutenant and below. Those who volunteer for active duty should apply to the Chief of Naval Personnel, Navy Department, Washington 25, D. C.

Qualified civilian physicians, dentists, and nurses may apply for active duty in the Medical and Dental Corps of the U. S. Naval Reserve and will be commissioned in ranks up to and including lieutenant commander for physicians and dentists, and up to and including lieutenant for nurses, depending upon age and professional experience. Interns in civilian hospitals are urged to apply for a commission in the rank of lieutenant (junior grade) in the Navy Medical Corps Reserve and have the remainder of their intern training sponsored by the Navy with pay. For additional information regarding commission and appointment, application should be made to the nearest Office of Naval Officer Procurement.

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Intravenous Administration of Tetracaine Hydrochloride: Tetracaine (pontocaine) hydrochloride, a higher homologue of procaine hydrochloride, was selected for clinical trial in the treatment for pain syndromes. It is dibutyl-dimethyl-aminoethanol para-aminobenzoic acid hydrochloride and is about ten times as potent and ten times as toxic as procaine on the basis of animal experiments. Tetracaine is used as a topical anesthetic and has proved efficacious in ophthalmic and otorhinolaryngologic work; it has been used extensively in caudal and spinal anesthesia; and Moore has reported the production of one hundred and fifty brachial plexus blocks with 0.15 percent solution of tetracaine, using from 80 to 125 mg. without evidence of toxicity but with satisfactory anesthesia for from 5 to 6-1/2 hours.

The author of this report had employed 0.15 percent tetracaine solution, using from 7.5 to 100 mg. of the drug, more than one hundred times in infiltrations and induction of nerve blocks, without any untoward reaction. This suggested that tetracaine might be given intravenously. Small amounts in great dilution were tried, then gradually increasing doses, until one patient received 250 mg. in 500 cc. of isotonic sodium chloride solution. This apparently massive dose had no undesirable effect. Because the purpose of the study was to develop an office procedure, the dose settled on as optimal was 10 cc. of 0.25 percent tetracaine solution, given slowly over a period of from 3 to 5 minutes. The patient is kept supine during the infusion and for about 5 minutes afterward.

The 0.25-percent solution is prepared by adding the contents of a 250 mg. ampul of tetracaine crystals to 100 cc. of isotonic sodium chloride solution. This solution can be kept in a rubber-stoppered bottle from which small amounts can be drawn as needed. The crystals should be dissolved in an isotonic solution rather than in distilled water. The injection can be conveniently made with a 25-gauge needle, which causes only slight venous trauma and facilitates slow administration; however, any needle suitable for intravenous use can be employed.

In this preliminary work, a series of 104 patients received a total of 204 intravenous infusions of tetracaine for treatment in arthritis, leprosy, muscle strain, lower back pain, asthma, and miscellaneous conditions, such as hyperactive carotid sinus syndrome, pain in the chest, and neuritis. One patient fainted and one patient had slight nausea and vomiting. Some have complained of transient dizziness. No other reactions have been noted. The administration of oxygen, barbiturates, or stimulants was not required. Of the 104 patients treated, 98 (94 percent) experienced definite improvement. Ages ranged from 15 to 80 years. Persons treated were Caucasian, Hawaiian, Negro, Filipino, Chinese, Korean, Japanese, and Portuguese; no difference in racial tolerance could be demonstrated. Most of the patients were workers on a sugar plantation seen in an industrial medicine practice. Some were patients or staff members at the Kalaupapa Settlement, Molokai, Territory of Hawaii, the center for the treatment of leprosy in Hawaii.

The effects of tetracaine given intravenously are similar to those of intravenously administered procaine, but the action is more prolonged and the result more pronounced. Tetracaine apparently has an affinity for inflamed or traumatized tissues, as well as an antispasmodic action. Its administration gives good results in spastic conditions of both smooth and skeletal muscle, as far as can be determined from the present study; spasm of skeletal muscle and bronchial spasm respond equally well to this treatment. In addition, tetracaine probably has an affinity for inflamed or hyperirritable nerves as shown by the good effects of its use in patients with hyperactive carotid sinus syndrome and various neuritides. Chiefly, it relieves pain, probably by an anesthetic effect on the nerve endings in any painful area. An antihistaminic action can also be postulated, although no laboratory proof is available as yet. The circulation is improved in the affected area by local vascular dilatation. These actions will be more apparent on consideration of the various conditions treated.

Asthma. Eleven patients were treated for asthmatic attacks, with a total of 22 doses. In all of them relief was immediate. One patient had not shown improvement after 2 doses of epinephrine, one intravenous injection of theophylline and inhalations of a mixture of helium and oxygen. He was finally given 10 cc. of 0.25 percent tetracaine solution intravenously and was free of respiratory embarrassment almost immediately. All the patients treated liked the method. In those who were treated at different times for more than one attack, response was uniformly good.

Arthritis. In the treatment for the milder types of arthritis limited to one or two joints, giving tetracaine intravenously proved efficacious; 20 patients with arthritis received a total of 38 doses, and the condition of 19 was improved. A 61-year-old Portuguese man who had been a constant visitor to the clinic for many years, a sufferer from chronic rheumatoid arthritis, was completely relieved after 5 injections. However, in most patients with rheumatoid arthritis, a better response will probably result from large intravenous doses of procaine.

Leprosy. Some of the minor complications of leprosy are benefited by the use of tetracaine. Eleven patients in this series were victims of leprosy. Five of these had intolerable itching, not relieved by treatment with antihistaminic drugs or other medicaments. These 5 reported cessation of itching, and in several relief lasted as long as 4 months. Two of the patients with particularly severe itching were given 100 mg. of tetracaine in 500 cc. of isotonic sodium chloride solution. One felt better almost immediately. The other, seen a few hours after the infusion, complained that the itching had moved from his back to his arms. The infusion was repeated on the following day and the itching disappeared. All 5 of these patients complained of a "deep" itch which was not relieved by surface scratching. This itch was so severe that the patients would pound themselves or each other until the skin became pulpy over the "itching" area. The literature on leprosy contains no reference to this "deep" itch, but it is probably a form of

neuritis of the larger nerve trunks, interpreted by the patients as itching. The remaining patients with leprosy were treated for various painful conditions, such as arthritis and painful neuritis. Of the 11 patients treated, 10 reported satisfactory results. A total of 28 doses was given in this group. Almost all these 11 subjects had some damage to the liver, and, as far as could be ascertained, the tetracaine treatment had no adverse affect. The use of tetracaine gives only symptomatic relief in leprosy and is not believed to have any effect on the course of the disease.

Pain in the Lower Part of the Back. Pain in the lower part of the back is one of the commonest complaints in a general or an industrial medicine practice. In all patients, gynecologic, urologic, orthopedic, neuritic, and mechanical causes should be ruled out. A great percentage of the patients with pain in the lower part of the back have no abnormal physical or roentgenologic findings. In many, the pain itself is the disease and no pathologic tissue changes can be found. Many of these pains in the lower part of the back respond well to local injections of procaine in the painful areas, or in the trigger zones, if any exist. However, the results are equally good with tetracaine given intravenously and the procedure is quicker. Eighteen patients received a total of 35 injections; of these, 16 reported improvement and 2 had no relief. Patients receiving this drug made fewer visits to the clinic and returned to work more quickly than those given the usual palliative treatment. The case report of a 56-year-old Filipino male janitor illustrates the efficacy of tetracaine treatment for pain in the lower part of the back. This man fell from a horse in July 1948. He reported severe pain in the left lower part of the back and in the posterior aspect of the left thigh. Roentgenograms of the spine showed no pathologic involvement. Myelograms were not made. Treatment consisted of the use of salicylates, heat and liniment. Four months after the injury, he was still complaining of pain and on examination was noted to have stiffness of the left lower part of the back, spasm and anesthesia on the lateral aspect of the left thigh and hypoactive left patellar reflex. A provisional diagnosis of herniated lumbar intervertebral disk was made. For the purpose of giving temporary relief, 10 cc. of 0.25 percent tetracaine solution was administered intravenously. The patient experienced immediate relief of pain. On the following day, examination showed that the spasm and anesthesia were no longer present. The patient was followed for a period of 8 months after treatment and he continued to be completely free of symptoms.

All but 2 of the patients treated expressed great satisfaction with the use of tetracaine and preferred it to such palliative measures as infrared radiation, diathermy and administration of salicylates. The number of visits per patient for pain in the lower part of the back decreased strikingly after tetracaine injections were started. The author states that he himself has taken 4 intravenous injections of tetracaine for such pain caused by a chip fracture of one of the lumbar vertebrae; relief lasts from 4 to 6 months. In the treatment for primary pain in the lower part of the back, intravenous administration of tetracaine seems to be more satisfactory than other methods. This is probably caused by the spasmolytic

and vasodilator effects of the drug, as well as the direct action of the tetracaine molecule on the irritated nerve endings.

Muscle Strain. Muscle strain of the upper and lower extremities often causes long-continued and disabling pain and stiffness. Ten patients were treated for muscle strain and 9 experienced relief. Whether the lesion is myositis, fibrositis, or calcific degeneration of muscle, relief is afforded by this method. A total of 13 doses was given. The condition in one patient was not improved and he preferred salicylates.

Miscellaneous. Thirty-four of the patients were treated for miscellaneous aches, neuritides and itching. These complaints ranged from pain in the chest following contusion to migraine headaches. Two patients had symptoms of hyperactive carotid sinus syndrome. They complained of dizziness and fainting on flexing or turning the neck and on bending forward. Pressure on the carotid sinus elicited the same symptoms. Each patient received one injection of tetracaine and had complete relief immediately. No recurrence was noted in either patient. This result suggests that the drug fixes itself to hyperirritable or inflamed nerve endings. Two of the patients had minor causalgia of several months' duration. The disease in both of them had been improved, but not completely relieved, by local nerve blocks; after intravenous administration of tetracaine the patients reported that the residual discomfort was so insignificant that they did not desire further treatment. However, without more conclusive evidence and further clinical trial, no statements can be made concerning the effect of tetracaine treatment in causalgia. Two patients with migraine headaches were treated. One was seen on the third day of the attack and tetracaine was used along with other drugs. No conclusions could be drawn. The other patient had been subject to weekly migraine headaches and on 2 occasions the headaches were aborted at the onset by the administration of 10 cc. of tetracaine solution. The remaining patients in this group were treated for painful scars, neuritis, itching, pleuritic pain, and burns. Pleuritic pain in 6 patients became less acute immediately. Itching was the chief complaint of 6 of the patients. One patient had Addison's disease; one had itching following a severe burn, and the other 4 had various dermatitides; in each the itching was relieved for periods of from one to three days. It is believed that tetracaine is an ideal drug for the control of intractable itching. Of the 34 patients in this miscellaneous section, 33 were improved; the remaining one was a nurse with dysmenorrhea of 3 days' duration. Forty-eight doses were given in this group. Some of these patients had been treated for a time with salicylates, diathermy, infrared radiation, liniment and other palliative procedures. After receiving tetracaine, most of them desired no further treatment. In the industrial medicine clinic, in which most of the tetracaine was used for pain in the lower part of the back, muscle strain and miscellaneous pains, the number of visits per patient decreased notably in 2 months.

The possibility of toxic reactions in the use of tetracaine exists and must be remembered. Some patients are sensitive to tetracaine, although none has appeared in this small series. As with the administration of any local anesthetic, three possible untoward effects must be looked for. One is allergy; the second is total vasomotor collapse, which has occurred following induction of nerve block and infiltration; and the third is the typical reaction to local anesthetization, which is ushered in by convulsions and excitement, and which proceeds to medullary paralysis and respiratory failure. If the solution is given rapidly, the danger is increased. It is axiomatic that a large dose of anesthetic can be given slowly with safety and that a small dose can cause trouble if given rapidly. In administering tetracaine intravenously, the patient should be watched carefully for any sign of untoward reaction and the injection should be made slowly. Any increased excitement, talkativeness, restlessness, muscular twitching, skin reaction,or dyspnea is an indication for immediate cessation of treatment.

All the patients reported on in this paper were watched carefully during the injection, and all received the drug slowly. If these two precautions are taken and the possibility of toxicity is kept in mind, unwanted effects will be minimized. (Arch. Int. Med., June '50, J. S. Horan)

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The Results of the Treatment in Active Minimal Pulmonary Tuberculosis with Modified Bed Rest: The problem of the proper treatment in minimal pulmonary tuberculosis is of growing importance because of the increasing number of minimal lesions being discovered by routine and mass roentgenography. Although bed rest has been the keystone of the treatment for this disease, there is much disagreement concerning the degree and duration of bed rest which should be employed. Strict bed rest seems to have the most support. Modified bed rest has been preferred by others. Finally, a combination of rest and exercise has also been recommended.

Modified bed rest is defined in this report as from 20 to 21 hours per day of reclining in bed or on a chaise longue, with meals eaten in an adjoining room, and full bathroom privileges. Riding or walking to other buildings for examinations was permitted, but no other outdoor exercise was allowed. Strict bed rest is defined as from 23-1/2 to 24 hours per day in bed, with the use of bedpans, stretchers for transportation to laboratories, and the like; 22 of the patients studied were so treated for from one to three months before admission to Trudeau Sanatorium but, because of its very limited use, this strict bed rest was regarded as modified bed rest for the purposes of this study.

This study was based upon a review of the records of all patients admitted to Trudeau Sanatorium between 1 January 1930 and 31 December 1940.

In 577 (22 percent) of the 2,612 patients admitted in these 11 years, the pulmonary lesions were classified as minimal at the time of admission to the sanatorium. These 577 patients were then studied clinically and roentgenographically from the time of admission through their sanatorium residence and the ensuing years until 1948. Serial roentgenograms were available to the writers in all but 26.

The purpose of the study was to observe the results of treatment in uncomplicated active minimal pulmonary tuberculosis. Certain of the 577 original cases were excluded for the following reasons: (a) 24 patients in retrospect did not exhibit conclusive evidence of tuberculosis, and were, in most instances, shown by subsequent events to have been incorrectly diagnosed; (b) 54 had advanced rather than minimal disease on admission, in the authors' opinion; (c) 76 had pleural effusion, either with or without minimal pulmonary infiltration; (d) 5 had a calcified primary complex only; (e) 11 cases were complicated by frank bronchial disease; and (f) in 11 cases the chief problem was some form of extrapulmonary tuberculosis. Thirty additional cases were excluded because advanced disease was found at some time prior to admission. Finally, 59 patients were excluded because the lesions were classified as inactive on the basis of the roentgenographic and bacteriologic criteria outlined below, in spite of the presence of suggestive symptoms in 45. The abnormal roentgen-ray shadows in these 59 patients were calcific in 9, stringlike in 29, mixed calcific and stringlike in the other 21; and these lesions remained unchanged during sanatorium residence in all instances. The lesions of the remaining 307 patients with minimal tuberculosis, exhibiting nodular or fluffy densities, were regarded as active, whether or not the shadows appeared inactive or stable on serial roentgenograms.

Sputum was considered positive when the clinical record revealed one or more sputum or gastric cultures positive for Mycobacterium tuberculosis, or one bacillus count of Gaffky II or higher on a smear of concentrated sputum collected over a 50-hour period. The finding of no more than from one to four acid-fast rods after a 20-minute search (Gaffky I) was arbitrarily disregarded as conclusive evidence of positive sputum for the purposes of this study. No direct smears of unconcentrated sputum, smears of gastric contents, or guinea pig inoculations were employed in this series. Sputum cultures were not regularly made until 1935; gastric cultures, not until 1939.

The results in all cases were then determined solely from the standpoint of reactivation of disease, as good, poor, or nonevaluable. A good result was defined as clinical and roentgenographic improvement, return to full-time employment, without reactivation of disease for at least 7 years following discharge from the sanatorium. (The number of sputum smears and cultures was inadequate in some cases, especially in the earlier years; hence a negative sputum on discharge is not included as one of the criteria of a good result. In fact, the last sputum prior to discharge was positive in 17 cases found to have achieved a good result.) A very minor or questionable increase in infiltration, not soon followed

by a more definite increase, was not in itself considered sufficient evidence of a poor result; this occurred in 15 cases. A poor result was defined as either progression or relapse of pulmonary disease. Progression was defined as the development of a cavity or a significant spread of disease, as shown in the routine chest roentgenogram at any time before the patient's return to full employment. Relapse was defin i as any reactivation of disease which led to a resumption of treatment either at home or in a sanatorium after return to full employment within 7 years following discharge. A 7-year observation period was chosen because, by 1948-1949, seven years or more had elapsed from the time of discharge of the last patients admitted in 1940.

A case not followed for 7 years was considered nonevaluable, provided no reactivation had occurred up to the time contact was lost. Eighteen of the 307 patients with active minimal disease were nonevaluable for this reason, 3 because of death resulting from nontuberculous causes in less than 7 years. This left 289 cases, the data concerning which were subjected to a statistical analysis.

After initial treatment with modified bed rest, the cumulative incidence of one reactivation or more during the period of treatment and for 7 years following discharge was 37 percent. The late results of modified bed rest treatment were favorable: only 3 percent of the patients had died of tuberculosis, and 4 percent were chronically ill with the disease in 1948 to 1949. Except for those dead from nontuberculous causes, those remaining were well and working at the last follow-up contact. There was a significant relationship between the incidence of reactivation and the following: the age of females, the estimated age of the lesion, the extent of involvement, the presence of symptoms, the time spent in the sanatorium, and the time spent away from full employment. There was no significant relationship between the incidence of reactivation and the following: the age of males, constitutional symptoms, the location of the lesion, one or more positive versus negative sputum findings, the rapidity and degree of clearing on serial roentgenograms, the presence of rales or elevated sedimentation rate on admission, and the duration of modified bed rest. There is need for controlled and comparative studies to assess the relative merits of modified bed rest, more lenient regimens, and the strict rest regimens used in the treatment for minimal pulmonary tuberculosis. (Am. Rev. Tuberc., June '50, R. S. Mitchell and J. R. Knudson)

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Radical Surgery in Cancer: Many physicians and surgeons have wondered and still wonder whether the radical surgery of today in the treatment of cancer is justified. The purpose in this paper is to try to discuss the subject objectively and from the experience of one who has lived before and has been living in a period of the most active development of this radical surgery.

The horizon of the extent and radical nature of the surgery for neoplastic disease has been for the past 30 years, and continues to be, a widening one in all the anatomical fields. The operative risk when many of these radical procedures were first attempted was high, but during the past 10 or 5 years, has been reduced to the 10- and 5-percent level. For example, in one municipal hospital, the operative mortality rate for gastric resections for ulcer 20 years ago was reported as 25 percent. During the past 5 years, the mortality rate has been 1.5 percent. The operative risk has similarly been reduced in many other procedures, such as lobectomy and pneumonectomy, resections of the cardia and esophagus, partial and total pancreatectomy, colectomy, and hemipelvectomy.

In evaluating the validity and justification of radical surgery in the treatment for cancer in its anatomical distribution and organ involvement, certain factors must be weighed; these are (1) the threat of the disease concerning life, dysfunction, and disability and distress, (2) the operative risk, (3) the probability of cure, (4) the assurance of relief of symptoms even though palliative and temporary, (5) the ability of the patient to adapt himself or herself or to tolerate dysfunction and deformity, inevitable in some of the radical procedures, (6) the quality of the resident staff in the essential pre- and postoperative care of the patient, and (7) the experience, skill, and integrity of the surgeon.

1. Threat of the Disease. Unless adequate therapy is given a patient with cancer, a fatal outcome is certain. In many such patients' dysfunctions, persistent, even intolerable pain and increasing disability are inevitable. Surgery is increasingly recognized as the most effective therapy in cancer, and must be radical enough to leave no residue.

2. Operative Risk. The operative risk is steadily decreasing in almost all of the radical procedures. When hemipelvectomy was first attempted, the operative risk was in the neighborhood of 40 percent; at a recent conference at the Memorial Hospital, 35 consecutive procedures of this type without an operative mortality were reported. In the first 10 years of radical pancreatoduodenectomy at the Presbyterian Hospital in New York, the mortality rate was approximately 33 percent in some 30 patients, whereas during the past 2 years, two surgeons reported 17 such consecutive procedures without an operative death. In Boston, 40 radical operations for ampullary carcinoma with only one death have been reported.

At the Memorial Hospital since September 1947, there have been approximately 200 cases of radical panhysterectomy with pelvic lymph node excision, with a surgical mortality of one patient (one half of one percent). These cases were unselected for size of lesion, local extension, age of patient, weight of patient, and nutritional status. There have been 62 complete pelvic exenterations, and among these there are 4 patients who have lived more than 2 years without evidence of recurrent disease and 3 patients who have survived for from one year to one year and 10 months without evidence of recurrent disease. This latter group was of the extreme advanced and hopeless type.

The reasons for these great improvements in various fields are a better understanding and intelligent use of transfusion, fluid and electrolyte balance; improved anesthesia; care in minimizing tissue trauma, and of improved technics; in better exposure and better wound repair; intelligent use of the chemotherapeutic and antibiotic agents; and, perhaps more important than any factor, the far more experienced and intelligent pre- and postoperative care of the patients in preventing operative and postoperative complications by the adequately trained resident staffs in the best surgical clinics.

3. The probability of cure and long-term survival. The salvage rate in the surgical treatment for cancer varies greatly, depending upon the type of tumor, the anatomic site, the limitation of spread, the radical nature of its removal, and the technical ability of the surgeon. Also, it depends upon the surgeon's understanding of the natural history and behavior of cancer, and the importance not only of removing it and its spreading pathways en masse, but of treating the patient as an individual human being and not merely as a case to be removed from a lump of cancerous tissue. The fungating type of carcinoma gives a better prognosis than the invasive, infiltrating variety, and remains localized for a longer period than the latter invasive type. Nevertheless, every cancer has individuality and is not altogether predictable. For example, carcinoma of the stomach is one of the most common and serious cancers encountered. The over-all salvage rate is low because of its insidious onset, its masking symptoms, its tendency to lymphatic spread (probably accelerated by the powerful contractions of its strong muscular coats), and the relative frequency of the invasive, infiltrative type of growth. The fungating type that mushrooms into the lumen and gives filling defects in roentgen-ray examination and a palpable tumor on palpation, is the more easily diagnosed at an earlier stage. But even today the medical profession is entirely too pessimistic on the one hand, and on the other hand in too many favorable cases, the patient is not sent to the surgeon until after the cancer has spread to the liver and extensively into the lymphatics. A recent follow-up review of the gastric resections for carcinoma at the Columbia-Presbyterian Clinic, showed that of 256 patients with gastric resection for carcinoma of the stomach, 56 are living 5 years or more without evidence of recurrence; 32 are living between 5 and 10 years, and 24 have survived 10 years or longer. One of these, whom the author resected, lived 21 years and died of cardiac disease. Of the 56 five-year survivors, 15 showed lymph node involvement. All of these specimens had been carefully reviewed and re-examined to confirm the original diagnosis.

At the Memorial Hospital, a study of the end results in the treatment of gastric cancer by Doctors Pack and McNeer gives the following facts in patients studied from 1916 to 1946:

a. The resectability rate for gastric cancer has shown progressive improvement for each succeeding period: 1916-1930, 2.9 percent; 1931-1936, 7.7 percent; 1937-1941, 26.2 percent; 1942-1946, 39.8 percent.

b. Of 75 patients surviving gastrectomy performed 5 or more years ago, 26 or 34.7 percent lived 5 years or more without recurrence.

c. The presence of perigastric lymph node metastasis of resected gastric cancers influences the end results of treatment. Those patients without nodal metastases had 42.8 percent 5-year survival without recurrence; those patients with proved nodal metastasis had 24.2 percent 5-year survival.

d. The operative mortality for subtotal gastrectomy for cancer has decreased with each succeeding surgical period: 1916-1930, 62.7 percent; 1931-1936, 33.3 percent; 1937-1941, 15.5 percent; 1942-1946, 9.6 percent. More than 80 patients in the period of 1937-1946 have had either total gastrectomy or transthoracic cardiectomy for gastric cancer.

e. Local serosal penetration resulting in fixation to adjacent organs whose removal is compatible with life may not be an unfavorable complication, perhaps because of the more radical operation that must necessarily be done. In this series of 16 patients with this complication who had these radical operations, 8 (50 percent) were living and well at the end of 5 years.

4. The assurance of relief of symptoms, even though palliative or temporary. Palliative surgery must not be justified in terms of months or years of survival, but rather by relief of intolerable symptoms, freedom from discomfort, and the ability to resume a relatively normal way of living. It is with this measure of well-being that the present radical surgery of pelvic evisceration for recurrent carcinoma of the cervix following repeated bouts of radiation therapy, with the recurrence localized to the pelvis, must be judged.

These patients have constant pain (requiring morphine), vesico-vaginal or recto-vaginal fistula, or both, and are permanent invalids, often bed-ridden, and have been pronounced incurable. Pelvic evisceration, including removal of the pelvic peritoneum and iliac lymph nodes, and requiring ureterosigmoidostomy and a wet colostomy necessitating a special Rutzen bag, has to be carried out; nevertheless, the author has seen 8 patients living one to two years after operation, all of them expressing satisfaction in living free from pain and carrying on their household duties. None of them gave evidence of recurrent cancer. These procedures are being done in Boston and New York with a steadily decreasing operative risk.

Many esophagectomies and pneumonectomies, as well as pancreatic resections for cancer, must be considered palliative. But relief from intolerable symptoms even for a year or two is certainly everyone's right, if it can be given with relative safety.

5. The ability of the patient to adapt himself or herself, or to tolerate the dysfunction or deformity inevitable in some of the radical procedures. This

problem involves the psychology of the patient. Fundamental is the ability of the surgeon and his associates to understand this psychology and to prepare the patient for the psychic trauma, and to train the patient and the family in the control of his or her dysfunction, particularly in the cases of patients requiring colostomies, extensive amputations, laryngectomies, and in women requiring hysterectomy or radical mastectomy. In the past, too many surgeons have paid too little attention to the psychologic and physical rehabilitation of cancer victims. A program for rehabilitating patients in these and other categories, physically and psychologically, has been organized at the Massachusetts General Hospital in Boston and at the Memorial Hospital in New York.

6. The quality of the resident staff in the essential pre- and postoperative care of patients undergoing radical surgery for cancer. Carefully selected residents, with adequate training for periods of from 4 to 5 years in general surgery, with an intelligent understanding of the adjuvants previously mentioned that have done so much to lower the hazard of surgery, are essential in any hospital attempting to do present day radical surgery. The postoperative period involves complicated processes of fluid and electrolyte imbalance and abnormal adrenal response. The syndrome of metabolic alkalosis with potassium depletion has only recently been described, but is a most important and serious complication in some of the radical and extensive procedures. It is now recognizable by serum potassium determinations and electrocardiographic studies and readily prevented or controlled by the administration of potassium. The well-trained, intelligent resident, aware of the recent advances in the prevention and treatment of complications, is the indispensable assistant of the surgeon doing this type of surgery. Such a resident is often more competent than a so-called specialist who has not had residency training in general surgery.

7. The experience, skill and integrity of the surgeon. The surgeon's experience determines his qualification for deciding the extent and radical nature of the surgery to be done and the care of the patient before and after operation. His experience determines his judgment in deciding on whom and when to advise it, and how to deal with patients, and with the families of patients, in advising them, for they differ individually in their reaction to such advice and to the way it is given. His skill determines to a large extent his ability to carry out difficult and hazardous surgery; this does not mean the speed with which he operates as much as the care of the tissues and the minimum trauma he inflicts in the doing of the surgery, and the repair he accomplishes, without puttering and wasting time.

His integrity is more difficult to define. It implies humaneness and kindly understanding in dealing with the cancer victim, his family and his problems, the ability to restore confidence and hope, and the desire to use infinite pains in caring for the patient. To have integrity, he must know his limitations and be willing to advise the patient to seek the services of a surgeon capable of handling the problem, if he himself is not qualified.

One of the hazards of radical surgery at the present time, especially in some of the newer procedures, is the tendency on the part of certain specialists without experience in the field of general surgery to visit a clinic where some of the extensive operations are being done, to see one or two such procedures, and then to return to their own clinics to begin this work. The results will unquestionably be calamitous but will not be published. This type of surgery cannot be learned from a surgical amphitheatre or by television, and should not be attempted by those who have not had adequate training and apprenticeship in general surgery, in the preoperative, the operative, and the postoperative care of patients subjected to such surgery. (Ann. Surg., June '50, A. O. Whipple)

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Evaluation of Chlor-Trimeton Maleate in Hay Fever and a Variety of Allergic Diseases: Clinical reports on chlorprophenpyridamine maleate, known also as chlor-trimeton maleate (Schering Corporation), have indicated that this potent antihistaminic substance benefits a large percentage of patients with hay fever to whom it is administered. The drug has also been shown to be of definite value in vasomotor rhinitis, urticaria, and other allergic diseases.

The effects of chlor-trimeton maleate were studied among 117 patients seen in office practice and in outpatient departments of certain hospitals by the author. The majority of the patients were suffering from hay fever. Other disorders for which these patients were treated included vasomotor rhinitis, allergic asthmatic bronchitis (with and without complications such as hay fever or vasomotor rhinitis, or both), atopic eczema, allergic migraine headache, neurodermatitis, pollen eczema, poison-ivy eczema, and angioedema with hives.

Patients under the age of 15 years were given 2 mg. of chlor-trimeton maleate 3 times a day. Each patient over 15 was instructed to take one 4-mg. tablet up to 4 times a day. If, at the end of the first day of treatment, there was no measurable response to the drug, the dose was increased to five or six 4-mg. tablets per day.

The results seemed to be less favorable in the patients who took the increased dosages than in those who could achieve a measure of benefit from 4 tablets a day. There was a notable absence of side effects. The patients who reported no improvement did not complain of drowsiness, nausea, or dizziness. They stated, rather, that they felt no benefit from the use of the antihistamine.

Hay Fever. This group of 58 cases included patients ranging in age from 5 to 65 years who were sensitive to tree, grass, and ragweed pollens. Symptoms were completely relieved in 49 cases, or 84 percent, of those treated. In 10 cases, placebos were substituted for chlor-trimeton maleate tablets after it had brought about the subsidence of symptoms. With placebos, nasal discharge and

other symptoms returned. When the patients subsequently were encouraged to try the drug again, these symptoms disappeared. Five patients among those benefited were able to maintain a complete cessation of symptoms throughout the hay-fever season with the use of 3 chlor-trimeton maleate tablets per day. Twenty-two of the 58 patients received chlor-trimeton maleate tablets, and placebo injections rather than desensitizing injections. These patients came in during the ragweed-pollinating season. The response in 18 of these 22 patients was both startling and highly gratifying, and they were able to go through the season without adjunctive therapy. The remaining 4 patients had severe hay fever unrelieved by the medication.

Vasomotor Rhinitis. This condition, nonpollen in nature, affected 25 patients. Treatment was successful in 18 cases (72 percent). In the 7 patients who did not obtain a satisfactory response, side effects were minimal. In 5 cases, the original benefit from chlor-trimeton maleate was lost when placebo tablets were substituted. Symptoms subsided again when treatment with the active substance was reinstituted.

Allergic Asthmatic Bronchitis, Uncomplicated. Of 5 male patients in the second and third decades of life with allergic asthmatic bronchitis, only one experienced any relief.

Allergic Asthmatic Bronchitis with Hay Fever or Vasomotor Rhinitis or Both. In 7 male patients, in the second and third decades of life, allergic asthmatic bronchitis was complicated by hay fever or vasomotor rhinitis, or both. Two reported relief of the asthma. Asthma and hay fever occurred in these patients during a pollinating season, and the author believes that the control of hay fever by chlor-trimeton maleate led to cessation of the asthma.

Atopic Eczema. In 2 children, aged 3 and 5 years, with eczema, regression of the lesions and cessation of the pruritus followed treatment.

Allergic Migraine Headache. Two female patients in the second and third decades of life who were suffering from migraine headache of allergic origin, were given the drug. In one of them there was a substantial measure of relief, although not total cessation of symptoms; the headache in the second patient was not relieved.

Neurodermatitis. In 5 (71 percent) of 7 patients, ranging in age from 18 to 60 years in whom neurodermatitis was present, the eruption subsided and pruritus was relieved. These patients were highly pleased with the results of the medication.

Pollen Eczema. In one of 3 adults in this group, pruritus ceased, and the eczematous lesions subsided. Very little improvement became apparent in the other 2 patients.

Poison-Ivy Eczema. Results were highly satisfactory in 2 patients treated for poison-ivy eczema; the itching stopped and the inflammation was reduced.

Angioedema with Hives. The hives disappeared in 5 (83 percent) of 6 cases after the administration of a few doses of chlor-trimeton maleate.

In addition to the beneficial effects obtained, the author emphasizes the almost complete absence of side effects. (New England J. Med., 15 June '50, N. E. Silbert)

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The Effect of Aluminum Hydroxide on Serum Aureomycin Concentrations After Simultaneous Oral Administration: Aureomycin is readily and completely adsorbed from aqueous solution by aluminum hydroxide, silica gel, charcoal, magnesium oxide and other well known adsorbents. It is also adsorbed from serum by silica gel. After adsorbtion from aqueous solutions or serum it is exceedingly difficult to remove the aureomycin from the adsorbent. Thus, aureomycin administered with aluminum hydroxide should be bound to the aluminum hydroxide and remain in the gastrointestinal tract. Waisbren and Hueckel measured the blood concentration of patients receiving aureomycin and reported a fall when aluminum hydroxide was given. (See Medical News Letter of 10 March 1950.) Aluminum hydroxide is frequently prescribed with aureomycin to relieve gastrointestinal symptoms. Experiments to determine quantitatively the effect of administration of aureomycin with and without aluminum hydroxide in normal individuals were undertaken.

Eleven mg. per Kg. of body weight of aureomycin hydrochloride in gelatin capsules was orally administered to 9 healthy subjects. Serum levels were measured at 2, 4, 8, 12 and 24 hours by adsorbing the aureomycin on silica gel columns and observing fluorescence. The same subjects, under the same conditions several days later, then took 11 mg. per Kg. of aureomycin and 0.3 ml. per Kg. of a commercial USP aluminum hydroxide gel preparation, and the serum levels were redetermined. All medications were taken at 8:30 A. M. Fasting subjects ate no breakfast but ate lunch between noon and 1:00 P. M. The amount of aluminum hydroxide corresponds to from 1/2 to 3/4 of an ounce, less than the amount recommended clinically in the treatment for gastrointestinal symptoms.

The results are reported in microgram-hours, because this measurement represents the sum of all blood concentrations for each instant of time following a single dose. Microgram-hours were determined by plotting serum levels against time and graphically measuring the area under the curve. When comparing 2 methods of administering a drug, and neither method has a significant effect upon the time-course of the blood concentration and there is considerable random variation in the time-course, a valid comparison can be made

only in terms of concentration-time units. Concentration-time units then give one a single figure representing a set of blood concentration data; a figure which allows a simple statistical comparison of different sets of data.

The data clearly indicate that aluminum hydroxide inhibits absorption of aureomycin from the gastrointestinal tract. The average number of microgram-hours of aureomycin after an oral dose of 11 mg. per Kg. is 13.7. After the same dose of aureomycin plus 0.3 ml per Kg. of aluminum hydroxide, it is less than 3.0. The average difference in microgram-hours produced by taking aluminum hydroxide with the aureomycin was 10.7. The most likely explanation of the difference in microgram-hours produced by giving aluminum hydroxide with the aureomycin is that the aureomycin is bound to the aluminum hydroxide and remains with it in the gastrointestinal tract. Thus it appears to be inadvisable to give aluminum hydroxide, except for the purpose of eliminating aureomycin from the body.

It was noted that women taking aureomycin without aluminum hydroxide had higher serum levels and more microgram-hours of aureomycin than men after the same per kilogram dose. The average number of microgram-hours for the women was 19.9, and for the men 10.4. The probability of this occurring on a random basis is 0.003. Such differences in serum levels between males and females were not apparent after taking aluminum hydroxide. The reason for this may have been that the concentrations after aluminum hydroxide is taken are at the limit of sensitivity of the method of determining aureomycin. Despite the fact that the number of subjects was small, this difference in serum levels between males and females is provocative and deserves further investigation. (Bull. Johns Hopkins Hosp., June '50, J. C. Seed and C. E. Wilson)

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Digitalis in Cardiac Disease Without Congestive Heart Failure or Auricular Fibrillation: Stress on the hazards of the use of digitalis during the last quarter century has led to an undesirable degree of limitation of its use and general rules have been well learned at the expense of exceptions that are as important. In restricting the use of digitalis to patients with congestive failure and auricular fibrillation, it is often withheld when it is much needed. Distrust of digitalis has been produced by such practices as: (1) improper use through fear of its effects; (2) forbidding its use in the presence of a normal heart, or in the absence of clear evidence of myocardial failure; and (3) ascribing to it most of the complications which may occur naturally in the course of serious cardiac disease. Fear of the drug may result paradoxically in such actual overdosage that the drug is condemned, or in such underdosage that confidence in its usefulness is destroyed.

Misuse by overdosage very often results from repeating the dosage too quickly instead of allowing sufficient time for the effects of each dose to take

place; it is possible to pour in an injurious quantity of the medicine before any of the signals for forbearance appear. With timidly given small doses, at short intervals of only 2, 3, or 4 hours, the last dose is often given well before the full effect of the preceding dose is apparent. Intoxication frequently results, increasing timidity in the use of the drug and giving rise to many mythical instances of sensitization to it.

What is thought to be a cumulative action of digitalis, after diuresis, from digitalis concentrated in the remaining extracellular fluid, seems more likely to be the cumulative effect of the last dose of digitalis given at too short an interval. This can easily occur when the fluid accumulation is so great as to cause mechanical embarrassment which keeps the pulse high, even though an otherwise full digitalis effect has been achieved by the dose preceding the last one.

The author's cases, managed on a high fluid regimen (especially when a mercurial diuretic is given), as a rule have a greater diuresis than those handled with a restriction of fluids. Yet he has never observed this phenomenon of cumulative intoxication, even though some of his patients have received more than the usual amount of digitalis for their weight and have exhibited the usual therapeutic response in the form of a slowing of heart rate and relief of dyspnea. However, symptoms and signs suggesting digitalis intoxication have been seen in cases in which a profuse mercurial diuresis induced hypovolemia. The signs and symptoms of this are easily relieved by a little extra salt and water, while digitalis is continued. There is actually no evidence that digitalis accumulates in the extracellular fluid; indeed embryonic duck heart assays suggest that it remains in the extracellular fluid less than an hour.

Simple overdosage intoxication may be brought about when some factor other than failure of the myocardium or auricular fibrillation is responsible for the elevated heart rate and dyspnea. Besides the factor of the mechanical effect of a large accumulation of fluid, one must recognize the effect of fever, of thyrotoxicosis, or of a severe anxiety state, and not expect digitalis to do what only the aspiration of fluid, an antipyretic, iodine or propyl thiouracil, or a sedative can do. In such cases it is best to give only an estimated digitalization dose and then a moderate maintenance dose until these complicating factors have been brought under control by other suitable means.

Misuse by underdosage is often the result of fear of the drug's effect in the presence of vomiting, diarrhea, or a slow pulse. If no digitalis has been given, one, of course, may confidently give it in an effective amount to a patient with obvious congestive failure in the presence of a pulse reduced to 30 by a coincident heart block. Likewise, one may achieve gratifying rapid control of vomiting by the use of digitalis by vein; notably in patients with auricular fibrillation, but also frequently in other cases in which anoxia affects the vomiting center in the brain or the gastrointestinal mucosa so as to produce repeated vomiting.

The situation which taxes courage and judgment is that in which, as a result of heart disease, the pulse may become very slow or vomiting appear in a patient who has been on a maintenance dose of digitalis or is in the very early stages of being digitalized. If the patient has not been seen for some time and has been on what was thought to be a maintenance dose of digitalis, one must always bear in mind that he may, in fact, be completely undigitalized. This is particularly true if the patient has not been seen for from 3 to 6 months. In that length of time, if one has only slightly underestimated the patient's maintenance dose, all real digitalis effect may have disappeared even though the patient has taken one or two doses every day. Often the patient has forgotten to take a dose or two a week, resulting in the loss of all digitalis effect; this can be demonstrated by comparing the number of tablets gone from his bottle with the number of days since he was last seen. In such case, the vomiting may disappear and the response be identical with the rapid administration of the same amount of digitalis that would be given had the patient not been on digitalis therapy. This is also true of the new patient who is in the very early stages of being digitalized.

Although digitalis has no effect on the heart rate in complete heart block with idioventricular rhythm, it will often prove to have a very beneficent effect on the myocardium, as evidenced by the relief of nocturnal dyspnea and of dyspnea on exertion, or of anoxic central vomiting, even in the absence of any evidence of gross congestive heart failure.

The second factor that has greatly limited use of digitalis is the belief that the functioning of a normal heart is impaired by its administration. This idea was based on work which appeared to demonstrate that the use of digitalis resulted in a reduced volume output in the normal heart. In the last few years, however, data concerning therapeutic dosage from newer technics applied in human beings and in animal experiments have been compiled which are in conflict with the older work. However, for fear of hindering the action of an apparently normal heart, digitalis is frequently withheld whenever gross abnormality of the heart is not obvious. This is partly because overdosage-misuse resulting in toxic, not therapeutic, dosages of digitalis in patients with pneumonia, thyrotoxicosis and circulatory collapse, gave digitalis such a bad name, that it is now often withheld in such patients when they might survive with its use.

Even in the absence of complicating disease it is often impossible to be sure that a heart is, in fact, normal. Only the results of a therapeutic trial of digitalis may reveal that myocardial disease or impairment actually does exist. Many such therapeutic trials have demonstrated that one can not arrive at the conclusion that a normal heart exists from the evidence obtained by auscultation, the electrocardiogram, circulation times, etc., in the very ill patient, especially when an all-important satisfactory history cannot be obtained.

In a certain number of these cases (for example, in pneumonia, now that pyrexia can usually be controlled quickly and one can more often use the indication of a tachycardia out of proportion to the temperature), one may see a gratifying and even life-saving response to a therapeutic trial of digitalis, indicating that under cover of the thyrotoxicosis or pneumonia or circulatory collapse there indeed existed, or had developed, an important degree of myocardial failure.

Formerly, patients in their fifth, sixth, or seventh decades of life with an adenoma of the thyroid without thyrotoxicosis, would all too often fibrillate wildly postoperatively and require rapid emergency digitalization. Their electrocardiograms had been normal and they had been carefully examined and interrogated by competent internists who had been unable preoperatively to detect any reason for the use of digitalis or for anticipating fibrillation. Now, such patients are usually digitalized preoperatively. Harmful effects or clinical evidence of reduced myocardial function pre- or postoperatively have not been detected, even though some of these patients undoubtedly have normal hearts. Of course, one can hurt any such patient by "pouring in," as Withering puts it, "an injurious quantity of the drug." But if this is avoided, it is believed that neither the fear of the effect of digitalis on a normal heart, nor one's inability in complicated cases to be sure of the presence of myocardial disease or myocardial insufficiency, should be allowed to interfere with a short therapeutic trial of a drug that might be life-saving.

In patients suffering with chronic pulmonary disease, the pulmonary findings often make it extremely difficult to decide whether or not some degree of pulmonary passive congestion or left ventricular failure exists as a result of recent or long-standing right heart strain. There are cases in which the differential diagnosis cannot be established by the usual tests. In the author's practice, digitalis is given a trial in most cases in which the patient is in really serious difficulty with asthma-like bronchitis, bronchiectasis, or in any other condition in which, after careful consideration, one suspects that the presence of an element of chronic cor pulmonale is responsible for some degree of symptoms and findings.

Furthermore, a therapeutic trial of digitalis should not be neglected in cases of acute or chronic Bright's disease or cirrhosis of the liver with edema and ascites. Advancing renal and hepatic disease syndromes are frequently associated with myocardial failure, and it is often difficult on the basis of examination or electrocardiography to judge at what point digitalis might be helpful. The drug has, moreover, been found by the author to be very useful in controlling disabling degrees of ventricular extrasystoles and of paroxysmal auricular tachycardia when congestive failure was not present and, indeed, when the hearts in these cases appeared to be perfectly normal.

Even if the results of such therapeutic trials are occasionally disappointing, no harm has ensued, in the author's experience. Such trials often yield

gratifying surprises to one who is humble enough to admit the difficulty in deciding whether a heart is normal or whether the early signs of heart failure are present. If one can put aside the idea that properly administered digitalis hampers the normal heart, its use on well-considered suspicion may prevent the development of the full-blown picture of congestive failure, left ventricular failure, or permanent auricular fibrillation. The commonly accepted criteria for the use of digitalis are as beautifully clear, and often are as late signs as cavitation and positive sputum are in pulmonary tuberculosis.

The use of digitalis has also been unjustifiably limited because almost every complication that occurs, in the course of observation in acute or chronic heart disease, has been attributed by some authority at some time to the use of digitalis. It is a fallacy to attribute the unfavorable events which may occur naturally in the course of heart disease to the use of digitalis, because any one with an adequate experience has seen all of these unfavorable events develop in cases of heart disease when digitalis was not in use. Auricular fibrillation and flutter; the presence of acute coronary occlusion with myocardial infarction; pulsus alternans, heart block, rupture of the ventricle, and the throwing off of emboli; not to mention ventricular tachycardia and ventricular fibrillation have all been attributed to digitalis. Nevertheless, assuming that digitalis is being skillfully used, neither the reasoning nor the data presented justify the conclusion that these symptoms are produced by digitalis.

In many texts and lectures, digitalis in the presence of myocardial infarction is only grudgingly conceded a place in the presence of fully established and grossly evident congestive heart failure or in the presence of auricular fibrillation with a rapid ventricular rate, or of rapidly progressing left heart failure. However, rapid digitalization is recommended by the author, along with oxygen in acute profuse pulmonary edema, which is so often precipitated by an acute myocardial infarction. In such desperate situations, which might have been prevented by earlier use of digitalis, the theoretical contraindications to its use, such as the production of ventricular fibrillation and rupture of the ventricle, are laid aside.

The advisability of freer use of digitalis in the presence of acute myocardial infarction is suggested by the fact that some two thirds of the patients who survive their myocardial infarction develop congestive failure in the hospital or shortly after dismissal. Furthermore, if one looks in detail for the signs and carefully inquires into the history, a considerable number are found to have been suffering with congestive failure when infarction occurred. Digitalis is given in such cases from the very beginning and in all cases in which the presence of myocardial failure is suspected. It is easy to overlook rapidly developing signs of failure in a patient who is tucked away in an oxygen tent and kept comfortable with opium. In the absence of signs of congestive heart failure, the author has not hesitated to use digitalis when a rapid, feeble, or irregular pulse and dyspnea persist, unrelieved by oxygen and morphine. He gives the digitalis slowly or

rapidly, by mouth or if necessary by vein, as he would in cases of ordinary congestive failure without complications.

The action of the drug on the non-necrotic portion of the myocardium appears to lead to improvement that may anticipate and prevent not only congestive failure, but also the development of the very disturbances of rhythm which are feared and which digitalis in toxic amounts may produce. Thus heart block may disappear with a general improvement which was apparently induced in part by rapid digitalization. Ventricular tachycardia following infarction, whose persistence in the presence of good doses of quinidine is producing rapid progressive failure, may come under control coincident to full digitalization. Rupture of the ventricle following infarction is commonly observed only in those who pursue accustomed activity in spite of the presence of a recent infarction.

Although one can harm or kill even a healthy man with injudicious use of digitalis, in the author's experience with acute myocardial infarction, complications (including the onset of ventricular tachycardia and the occurrence of sudden death) appeared as often in those patients who were not receiving digitalis as in those who were receiving it. In a series of 265 consecutive cases, his first-admission mortality rate was 10 percent, compared with that of 16 percent in a similar series of 286 cases. This suggests that the use of digitalis was not strikingly harmful, and may well have been beneficial. Many patients with very unpromising cases in this series had failed to respond to rest, opiates, and oxygen, but responded to digitalis in therapeutic doses, when it was used as if an acute myocardial infarction were not present.

The use of digitalis in all of the disturbances of rate and rhythm except auricular fibrillation is usually frowned upon, at least until congestive failure develops. Yet the author has occasionally found it to be very useful in any of these disturbances, including those in which only quinidine is customarily sanctioned. In all of these types, especially in the more desperately ill, instances were noted in which the disappearance of the arrhythmia coincided with improvement in myocardial function. This improvement appeared to be brought about, at least in part, by a free use of digitalis. In milder types of these disturbances, such as ventricular extrasystoles or paroxysmal auricular tachycardia which have become disabling, the use of digitalis may result in their control and the relief of attendant anxiety states or disability; this is often seen after a suitable control period of confident reassurance, hygienic advice, and adequate sedation has proved entirely ineffective. In older patients, control of paroxysmal auricular tachycardia with digitalis may prevent the precipitation of myocardial failure or myocardial infarction. (No reference is made to the transient T wave changes, which, even though they are belittled, do indicate the appearance of as much disturbance as is considered significant, for example, in an exercise tolerance test.)

In disabling degrees of ventricular extrasystoles, the firmest verbal reassurance to the patient must be accompanied by relief of symptoms in order to

overcome an anxiety state or cardiac neurosis. This relief can occasionally be achieved only by the temporary or continued use of digitalis or quinidine. In the author's experience,the digitalis is usually quite as effective as quinidine and a little bit safer. If, occasionally, extrasystoles or incomplete heart block is made worse by digitalis, no harm has come of a properly carried out and observed therapeutic trial, in which the drug has been given at intervals of from 12 to 24 hours and has been promptly withdrawn upon the appearance of unfavorable signs or symptoms.

The more serious disturbances of rhythm or rate, heart block (with or without ventricular asystole), or ventricular tachycardia, are often signs of as grievous a myocardial injury as is a true gallop rhythm. In the author's experience, digitalis may at least tide the heart over until the harmful disturbance stops spontaneously, or it may, through effecting a general improvement in myocardial function, actively help to re-establish a normal rhythm. In any event, the same disturbances of rate and rhythm (including ventricular tachycardia), which may develop when digitalis is given in toxic amounts, have disappeared with the use of full therapeutic amounts of digitalis, in cases in which these disturbances have been produced by some other form of myocardial injury such as infarction of the myocardium.

It must be pointed out, however, that even the traditional indications for digitalis have their exceptions. As more is learned of the role of sodium in congestive heart failure, patients are being seen in the severest congestive failure who have so little real myocardial insufficiency that their edema clears with simple sodium regulation without the use of digitalis. Likewise, patients with auricular fibrillation with slow ventricular rates often do well for years without digitalis.

In addition to those factors outlined which have led to the condemnation of digitalis as dangerous and unmanageable in many conditions in which it is useful, the influence of the electrocardiograph should be mentioned. Its tracings are not as good guides for the continuation or withdrawal of digitalis as are clinical indications, and there is often confusion concerning the difference between digitalis intoxication and digitalis effect which may lead to unjustified withdrawal or, on the other hand, to the unwise continuation of the drug. (Postgrad. Med., June '50, F. R. Schemm)

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Preliminary Report on the Possible Role of the Adrenal Cortex in Cardiac Edema: It would seem that the altered physiologic changes that occur in sodium and water metabolism in congestive heart failure might in some way affect or be affected by adrenal cortical function.

The effect of various types of body stress on adrenocortical function has been well demonstrated by Selye. It therefore seems reasonable to conjecture

that impaired cardiac efficiency might constitute a form of chronic stress, in which case the adrenal cortices would respond by a moderate but continued stage of counter shock or resistance of the adaptation syndrome resulting in a prolonged overproduction of adrenal cortical hormones. If this were true, adrenocorticosteroids concerned with sodium and water metabolism might profoundly influence, and perhaps even be, the primary factor in the retention of sodium and water which occurs in congestive failure.

In 1910, a method for estimating the circulating eosinophils was reported by Dunger, and his method was slightly modified and used in ACTH studies by Forsham, Hills, et al. Since then, it has been widely used and has been shown to be a fairly reliable index of adrenocortical function when determined in a serial manner or following injection of ACTH. Thus a continued fall or rise seems to parallel adrenal cortical secretion of hormones having, in most instances, salt-retaining and other effects. The level of circulating eosinophils varies widely in normal individuals and, except when allergic conditions are present, average values are decreased in hyperadrenal corticalism (Cushing's type) and increased in adrenal insufficiency of primary (Addison's disease) or secondary nature (Simmonds' disease). Therefore, the frequent determinations of the eosinophil levels during the course of improvement as the result of treatment in congestive failure appeared to be a promising study.

Eight patients with typical congestive failure were selected from 4 different institutions, and the blood studies done in the individual laboratory by different technicians. A basal eosinophil count was determined on the admission of each patient, and thereafter during the usual course of treatment for congestive failure. Because most patients with congestive failure experience the greatest improvement in the first days of treatment, eosinophil estimations were taken during that period. Eosinophil counts were made by the Thorn, Forsham, Hills modification of Dunger. In all patients the same program of treatment was used, i.e., mercuhydrin, salyrgan, theophylline, digitoxin, ammonium chloride and a low sodium acid-ash diet. Fluid intake and output and daily weights were recorded.

In all cases the initial eosinophil level was low, as compared with the normal average level of between 150 and 180 per cubic millimeter. As diuresis was instituted and continued by the above methods, periodic eosinophil determinations revealed a steady rise which in most cases reached normal levels in a few days. In every case, the loss of body weight closely followed the rise of circulating eosinophils. In addition, the relief of dyspnea and the return of general comfort to the patient were closely paralleled by the rising eosinophil level. In two cases, inadequate mercurial dosage failed to cause a significant diuresis and the eosinophil level remained low during this period. The physical evidence of congestive failure remained unaltered in these cases until increased mercurial dosage as well as digitalization was employed. Subsequently, both

patients rapidly improved, appetite was restored, and there was a sudden and marked rise in the eosinophil levels.

In those cases in which hematocrit and blood count determinations were done before and during treatment, the changes were not great enough to indicate that hemoconcentration played any part in the changes of eosinophils observed.

The consistent results obtained from these patients are of unusual interest. If the fluctuations of eosinophils are an indication of adrenal cortical activity, it appears from this study that there is corticosteroid hyperactivity in congestive heart failure which returns toward normal with the relief of failure; the latter may in itself constitute body stress. Whether such is the initial stimulus is a matter of conjecture. Further observations and investigation are being pursued along lines suggested by this study. (Lahey Clin. Bull., April '50, J. M. Elliott)

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Antibiotics in Typhus and Typhoid Fevers: The significant advances which have been made in the last 2 years in the treatment for the rickettsial diseases and for typhoid fever are reviewed. The findings that chloramphenicol and aureomycin are highly specific therapeutic agents for the rickettsioses and that chloramphenicol occupies a similar place in the treatment for typhoid fever have, for the first time, provided means for the adequate care of patients with these diseases. Both chloramphenicol and aureomycin display a marked rickettsiostatic effect in experimental animals infected with the rickettsiae which cause disease in man. These antibiotics may, under certain circumstances, have some limited rickettsiocidal effect, but this type of action does not appear to be the important or frequent means by which experimental infections are influenced. Furthermore, there is evidence from the laboratory that chloramphenicol, at least, has no direct effect on the rickettsial toxins. Clinical evidence appears to coincide with and supplement the observations which have been made in experimental animals infected with rickettsiae and treated with either of these antibiotics.

Scrub typhus in man appears to be brought under control more promptly by chloramphenicol and by aureomycin than are the other rickettsial infections. The administration of either antibiotic results in prompt defervescence by crisis, the patient generally becoming afebrile within about 24 hours, whether treatment is begun during an early or late stage in the disease. The response seems to be equally good whether either of the drugs is given in a single oral dose of from 3.0 to 4.0 Gm. or whether following such an initial dose, the antibiotic is given in 0.25 Gm. amounts at from 2- to 3-hour intervals for another day or so. A few patients who were moribund at the time treatment was begun required 2 or 3 days of treatment before their temperatures returned permanently to the normal range.

Patients with scrub typhus continue to have demonstrable rickettsiae in their blood for a period of from 30 to 40 hours after treatment is instituted; in fact, rickettsemia continues for 12 or 24 hours after the patient has become afebrile and asymptomatic. Relapses of scrub typhus have only been encountered among volunteers who were purposely exposed in hyperinfected areas of scrub typhus during the course of chemoprophylactic tests. Such relapses occurred after about a week or ten days of apparently satisfactory convalescence, and responded promptly when treatment was again instituted. Recent work has shown that relapses can be prevented in these volunteers if a supplementary dose of either antibiotic is given on the eighth or ninth day after onset of fever. (i.e., about 6 or 7 days after the first course of drug was given which had resulted in prompt defervescence).

Such clinical observations support the thesis that the action of chloramphenicol and aureomycin is rickettsiostatic rather than rickettsiocidal. Ultimate recovery of the patient, be he mouse or man, depends on the development of host immunity. Convalescent animals and men continue to harbor living Rickettsia tsutsugamushi for appreciable periods of time.

In the other rickettsial diseases the 2 antibiotics are almost as effective as in scrub typhus. The average duration of the febrile phase in patients with Rocky Mountain spotted fever who receive either type of therapy is only 2 and a fraction days. The responses in epidemic and murine typhus are usually intermediate between those of scrub typhus and spotted fever. (The usual febrile period in untreated and uncomplicated cases of epidemic, murine and scrub typhus and in spotted fever is 14 days.) It is somewhat more difficult to evaluate the new drugs in patients with Q fever and rickettsialpox. Q fever varies in severity and rickettsialpox is mild. However, the rickettsia in both are quite susceptible under experimental conditions to the antibiotics, and the available clinical results are highly encouraging.

Field trials have shown that chloramphenicol can be used as a chemoprophylactic agent in human beings exposed in hyperendemic areas of scrub typhus. When the drug was given in daily oral doses of 1.0 Gm. during the 9-day period of exposure and for 12 days thereafter, clinical evidence of rickettsial infection was suppressed throughout the period and for about a week after the last dose had been given. At the end of this time scrub typhus developed in members of the test group. Eventually, the incidence of infection in those who had received prophylaxis was about the same as in the control group, in which disease had appeared at an earlier period. This prophylactic regimen neither prevented infection nor did it eradicate infection; it merely suppressed the clinical disease during the period of prophylaxis and for a short time thereafter. Subsequent studies showed that if prophylaxis were continued for a period of 4 weeks after exposure, the typical clinical disease was suppressed in volunteers while the drug was being taken and did not develop when the drug was stopped. The more prolonged regimen of 4 weeks' duration suppressed

overt disease in practically all members of the test group during the period when the drug was given, but during this time there was sufficient multiplication of rickettsiae so that an immune response was elicited. If the individuals had not become immune then they would have developed scrub typhus at the end of prophylaxis, just as had those volunteers in the tests in which prophylaxis was given for only 2 weeks.

The chemoprophylaxis of scrub typhus is of some practical importance, because a satisfactory vaccine is not available for protection against this disease. Chemoprophylaxis of certain of the rickettsial diseases which occur in the United States, e.g., Rocky Mountain spotted fever, is theoretically feasible, but it is not likely to be used, because preventive measures in current use are more suitable and practical.

The fact that specific therapeutic agents are now available for the treatment for the rickettsial diseases should not preclude the vigorous use of the classical measures for the prevention of the rickettsial diseases of man, i.e., vaccination and control of arthropods, when one is dealing with a group of persons who are exposed to grave risk of infection. On the other hand, these preventive measures are now used widely for persons who are only occasionally exposed to slight risk for short periods of time. In the author's opinion, preventive measures can be dispensed with for these persons at slight risk. If infection should occur, it could be promptly controlled with the available antibiotics.

During the first 2 days of treatment in typhoid fever with chloramphenicol, no obvious benefit can be noted in the patient's general condition. At the end of this time the temperature begins to drop by lysis and on the third or the fourth day it reaches a normal level and remains there. Convalescence usually proceeds uninterruptedly. Salmonella typhosa disappear promptly from the blood of patients following treatment; the organisms are usually not demonstrable as early as 2 hours after initial dose of drug. When therapy is given early in the disease before S. typhosa have appeared in the urine and feces, the disease usually abates without organisms ever being found in the excreta. In those who are treated later in the course of the illness, the typhoid organisms usually disappear from the stool and urine within a few days after the beginning of treatment but may reappear sporadically in about a third of the cases during the next several weeks.

It should be emphasized that the typhoidal lesions of the intestine do not heal immediately after therapy is instituted; time is required for this just as it is required for the resolution of the hepatized lung in the patient with pneumonia who is treated with penicillin. Intestinal hemorrhage and perforation may occur even after the patient has begun to improve; in fact, these complications have been observed in several instances in patients who had already become afebrile.

Such complications, however, are usually encountered during the first week after treatment is begun. Their incidence in treated patients is about the same as in untreated persons with this disease.

The other common complication of typhoid fever is relapse of the disease or recrudescence. The author has observed a close correlation between the duration of treatment and the incidence of relapses. All of the relapses which were observed occurred in patients who were treated for a period of 8 days or less. Seven of 13 patients with typhoid fever who were treated with chloramphenicol for an average of 6.9 days suffered a relapse. On the other hand, no relapses occurred in another group of 19 patients in whom treatment was continued for from 9 to 14 days, average 11.2. Similarly, no relapses were encountered in the third group of 12 patients whose therapy was continued for from 14 to 23 days, average 18.0.

In the group of 45 patients with typhoid fever who were treated with chloramphenicol there was one death; a boy 10 years of age died on the fourth day of treatment which was the eighteenth day of disease. He suffered several severe intestinal hemorrhages and received 2 blood transfusions during the course of therapy. In addition to evidence of bleeding, he was found, at autopsy, to have a perforated lesion of the ileum.

Rather extensive clinical trials have indicated that chloramphenicol is of no value in eliminating the typhoid carrier state in human beings. Although it is true that S. typhosa disappear from the bile of chronic carriers during treatment, nevertheless, organisms reappear promptly when the drug is discontinued. Perhaps the failure of chloramphenicol to benefit the typhoid carrier should have been anticipated. Tests in vitro show that solutions containing large amounts of chloramphenicol have no bactericidal effect against the typhoid organism. Concentrations of 1000 gamma per ml, which is 10 times the concentration ordinarily obtained in the blood of patients, stop the growth of S. typhosa but do not kill them. That chloramphenicol is a good therapeutic agent in the acute disease but of no value in the chronic carrier state, is, in the author's opinion, analogous in many ways to the situation in scrub typhus. In both the rickettsial and the bacterial disease the drug stops the growth of the organism, but does not kill it. During the period when the infecting agent is suppressed, the patient develops immunity by the usual processes. Thus having developed resistance, he is able to control the organism sufficiently to prevent clinical signs of disease, even though the organism persists in the body. Occasionally, multiplication of the organism within a given cell in the immune infected host may proceed to the stage in which it kills this particular cell, with the result that the organism is liberated. If this occurs in the convalescent scrub typhus patient and the organisms are dispersed within the patient's body, the neutralizing substances and other mechanisms prevent generalized infection. A similar situation might occur in the typhoid carrier if the ruptured infected cell liberated the bacteria into the tissues. On the other hand, the typhoid carrier sheds organisms through the

excreta into the external environment. The immune state of the typhoid carrier might be capable of controlling any bacteria liberated internally, but would not be able to affect those excreted. Thus, under this hypothesis, there is an important fundamental difference between the convalescent scrub typhus patient and the typhoid carrier. The former sheds his rickettsiae into his own body, whereas the latter sheds his bacteria outside. The factor which determines whether the person is a hazard to the public health is, therefore, the ultimate disposition of the organisms liberated from the cells of the resistant individual. (Am. J. Tropical Med., May '49, J. E. Smadel)

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Simultaneous Immunization of Young Children Against Diphtheria, Tetanus, and Pertussis: The chief reason for early immunization of infants is to confer protection against pertussis; neither diphtheria nor tetanus is a health problem during the early months of life. Approximately one half of all pertussis deaths occur before the seventh month. Reduction of these deaths to a minimum requires the administration of potent pertussis vaccine in sufficient dosage, as early in life as adequate and durable basic immunity can be conferred. Prophylactic use of pertussis vaccine earlier than the sixth month is desirable, especially for many infants in cities and institutions. If, in addition, it is possible to confer simultaneously adequate and durable basic immunity against diphtheria and tetanus, time will not only be saved, but discomfort and reactions will also be reduced to a minimum. It is important, however, that multiple antigens cause no untoward reactions, and that, when mixed, no one constituent lessens the antigenic potency of the others. Most cases of tetanus encountered in pediatric practice occur from insignificant wounds. There is no natural immunity. A multiple antigen containing tetanus toxoid confers protection to many children who would not otherwise receive it. For sustained protection after basic immunization against diphtheria, tetanus and pertussis, stimulating doses are necessary from time to time.

Because the value of early immunization is still an unsolved problem, further investigations seemed advisable. In a previous paper, the authors of this report pointed out that when the customary 3 doses of an alum-precipitated mixture of diphtheria toxoid and pertussis vaccine were administered during the first months of life, adequate pertussis immunity did not result. The present study was begun by administering 3 monthly doses of an alum-precipitated mixture of diphtheria toxoid and pertussis vaccine to a small group of infants, starting at the fourth month of life. Schick tests, diphtheria antitoxin determinations, and pertussis complement-fixation tests were performed 3 months after the final dose. The data showed that protection against diphtheria occurred in 97 percent, but only 65 percent of the infants showed adequate protection against pertussis. Because of these findings, the authors began to administer 4 monthly doses of an alum-precipitated mixture of diphtheria and tetanus toxoids with pertussis vaccine to a group of infants, starting at the age of 3 months.

This report is concerned with the results of administration of an alum-precipitated mixture of diphtheria and tetanus toxoids with pertussis vaccine to 2 groups of infants. Group I consisted of infants 6 or more months of age who received 3 monthly doses of 0.5 ml of the antigenic mixture. Group II were infants who received 4 monthly doses of 0.5 ml at 3, 4, 5, and 6 months of age. Tests for immunity were performed 3 months after the final dose of multiple antigens. The alum-precipitated mixture of diphtheria and tetanus toxoids with pertussis vaccine used in Groups I and II was a combination of refined diphtheria and tetanus toxoids and Phase I pertussis vaccine (Parke, Davis & Co.). It was standardized to contain in each ml of antigen twice the necessary amounts of diphtheria and tetanus toxoids and 30,000 million Hemophilus pertussis bacilli, so that amounts could be administered in doses of 0.5 ml each. The alum-precipitated mixture of diphtheria toxoid and pertussis vaccine used in the first study mentioned above was a mixture of standard alum-precipitated diphtheria toxoid and Phase I pertussis vaccine. The final volume of the product was standardized to contain twice the necessary amount of diphtheria toxoid and 30,000 million pertussis bacilli per ml. Both antigen preparations met the minimum requirements established by the National Institutes of Health.

Twenty-five gauge needles, from 10 to 15 mm. long were used. Each dose of 0.5 ml was administered deeply into alternate gluteal areas, starting with the left proximal region. To rid the needle tract of alum particles, each dose was terminated with 0.1 ml of air. As soon as the needle was withdrawn, the site was massaged gently and briefly with sterile gauze to prevent oozing, and to distribute the alum-precipitated antigen into the deeper tissues.

At the time of the first dose the parent was instructed to avoid excessive bed covering, to offer plenty of drinking water, to reduce the amount of food at the following meal, and to give one grain of aspirin one or more times daily if fever occurred. Systemic reactions were transient; occasionally the rectal temperature reached 39° C. within from 4 to 12 hours after injection. It was not necessary to subdivide or delay a dose on account of severity of systemic or local reaction. The preparation was not administered during an acute infection, in prematurely-born infants, in instances in which the physical condition made it inadvisable, or in any child with a tendency to convulsions (such as spastics). In no instance did a child develop convulsions or show any signs of encephalopathy. In some infants, a residual nodule could be palpated at the time of the subsequent dose. A fluctuating or discharging alum cyst was rarely encountered - approximately once in 800 doses.

Preliminary immunity tests were not performed before the administration of these alum-precipitated antigens because in previous studies it had been found, on the basis of immunity tests, that few infants at the age of 3 or 4 months possessed immunity to tetanus, diphtheria, and pertussis. Passive diphtheria immunity transmitted from the mother was usually absent.

Laboratory tests and skin (Schick) tests were used as evidence of antigen-conferred immunity because cases of diphtheria, tetanus, and pertussis have not been very frequent since 1940 in the area where this work was performed. No private patient injected with this multiple antigen prepared during the past 5 years is known to have contracted any of these diseases. The tests were made approximately 3 months after the final dose of multiple antigens. In both Group I and Group II, an antitoxin level of 0.1 unit or more per ml of blood was considered evidence of adequate immunity to tetanus. In Group I, a negative Schick test served as evidence for immunity to diphtheria and a complement-fixation reaction of 3+ or 4+ was considered evidence of adequate immunity to pertussis. For Group II, a negative Schick test and a diphtheria antitoxin level of 0.2 unit or more per ml of blood were considered evidence of adequate immunity. For pertussis, the rapid agglutination test of Daughtry-Denmark was used. An agglutination reaction of 3+ or 4+ was considered evidence of adequate immunity. This equals a titer 1:320 or more. Lapin described this rapid agglutination method in detail in his book Whooping Cough. The authors of this study employed the test because they had found good correlation between it and a tube agglutination method, and the more time-consuming complement-fixation reaction. When the result of a test indicated inadequate protection, a stimulating dose of 0.5 ml of the antigen was administered; when the child was retested a month later, the immunity response was usually found to be adequate.

Approximately 3 months after the final dose, follow-up tests for immunity were performed on 98 of the children, to whom 3 monthly doses of 0.5 ml of the alum-precipitated mixture of diphtheria and tetanus toxoids with pertussis vaccine had been administered after the sixth month of life (Group I). The Schick test was found negative in 100 percent; a tetanus antitoxin level of 0.1 unit or more per ml of blood was found in 96 percent; and the pertussis complement-fixation reaction was 3+ or 4+ in 83 percent. Infants whose tests indicated inadequate protection were given an extra (fourth) dose of 0.5 ml of the alum-precipitated mixture in the right distal gluteal area. A month later, the pertussis immunity had risen to an adequate level in each of the retested children.

Tests for immunity approximately 3 months following injections were performed on 163 children to whom 4 doses of 0.5 ml of the alum-precipitated mixture of diphtheria and tetanus toxoids with pertussis vaccine were administered at 3, 4, 5 and 6 months (Group II). The Schick test was found negative in 100 percent; a diphtheria antitoxin level of 0.2 unit or more per ml of blood was found in 100 percent; and the pertussis agglutination test showed adequate protection in 98 percent. (Am. J. Pub. Health, June '50, L. W. Sauer and W. H. Tucker)

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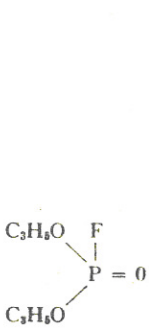
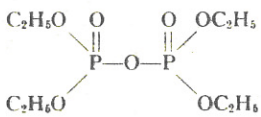
Uses and Hazards of the Organic Phosphate Anticholinesterase Compounds: Several esters of phosphoric acid are potent inhibitors of the cholinesterase (ChE) enzymes which are present in practically all animal tissues.

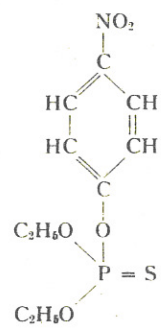
Lange and von Krueger were the first to note the high toxicity of one group of these esters, the alkyl fluorophosphates, which includes di-isopropyl fluorophosphate (DFP). The effects of DFP were found to result from its ability to inhibit ChE enzymes irreversibly. Thus, DFP could be used in the study of the role that ChE enzymes play in normal function and in disease. DFP has also been useful as a therapeutic agent in a number of situations in which a cholinergic effect is desired, as in the management of abdominal distention, of urinary retention, and of glaucoma. Another organic phosphate compound, tetraethyl pyrophosphate (TEPP), has proved to be of value in the management of some patients with myasthenia gravis. The usefulness of these compounds in therapy has been limited by the relatively narrow margin between the doses which are therapeutically effective and the doses which are toxic. The toxic effects of the organic phosphate compounds in animals of all species have led to the widespread use of some of these compounds as agricultural insecticides. These new insecticides, which are more effective than DDT, include p-nitrophenyl diethyl thionophosphate (parathion), TEPP, and hexaethyl tetraphosphate (HETP), The effects of HETP result from TEPP, the chief active product of its initial hydrolysis.



DFP



TEPP



Parathion

Studies performed in experimental animals have shown that almost all the pharmacologic effects of DFP, TEPP, HETP, and parathion can be explained in terms of their anticholinesterase (antiChE) action. By inhibiting the ChE enzymes which normally hydrolyze acetylcholine, these compounds cause the accumulation of acetylcholine and resultant cholinergic effects. Differences in their effects can be interpreted in terms of differences in solubility, degree of antiChE action, rate of hydrolysis and detoxification, reversibility of the ChE-antiChE combination, and rate of restoration of ChE enzymes in the tissues. Although parathion has lower antiChE activity and toxicity than TEPP, HETP, or DFP, there are at least two factors which are responsible for its greater efficiency as an insecticide. Unfortunately, these same factors are also responsible for the greater danger to man and domestic animals associated with the use of parathion. First, the rate of hydrolysis of parathion is much slower than that of the other antiChE compounds, 120 days being required for 50 percent hydrolysis of parathion at 25° C. and pH 7. Hence, once parathion has been sprayed on plants it may remain active for weeks, in spite of contact with moisture, in contrast to TEPP which hydrolyzes within several hours. Second, parathion is very much more soluble in lipoid than in aqueous media; this property may influence its persistence in the waxy outer layer of fruit and leaves, its absorption through the skin, and the degree of its central effects.

The organic phosphate antiChE compounds which are now in use may be absorbed through the skin, respiratory tract, conjunctivae, gastrointestinal tract; or following injection. Because these compounds do not produce local inflammatory changes in the skin, absorption by this route may be undetected until symptoms begin. Exposure may occur during the production, packaging, or handling of any of the compounds, during the spraying of insecticide preparations of parathion, TEPP, or HETP, or as a result of the harvesting or ingestion of fruit or vegetables on which they have been sprayed and which have been insufficiently weathered and washed. Exposure to TEPP during its use as an insecticide has resulted in several instances of severe but not fatal intoxication. Exposure to parathion during its production and use as an insecticide has resulted in the death of at least six men, and moderate or severe, but not fatal symptoms in at least 34 men and women. There have been recent reports of a larger number of fatalities and of severe intoxication attributable to parathion that have occurred in Brazil.

The effects of the organic phosphate antiChE compounds in man have been similar, in general, and are believed to be caused almost entirely by the inhibition of the ChE enzymes in the tissues, although an additional pharmacologic effect of parathion has not been excluded. The signs and symptoms produced by these compounds include muscarine-like, nicotine-like, and central nervous system effects that are attributable to the accumulation of acetylcholine in the tissues. The first muscarine-like symptoms to appear are usually anorexia and nausea. These are followed by vomiting, abdominal cramps, excessive sweating and salivation, and usually some degree of pupillary constriction. If the exposure is marked, diarrhea, tenesmus, involuntary defecation and urination, pallor, pin-point nonreactive pupils, blurred vision, excessive bronchial secretion, sometimes respiratory difficulty (suggestive of bronchoconstriction) and pulmonary edema with cyanosis follow. The blood pressure may be elevated during parathion-caused severe intoxication. Of the nicotine-like effects, the earliest are muscular fasciculations in the eyelids and tongue which may spread to the face and neck and to the extraocular muscles, resulting in jerking movements of the eyes. If the exposure is marked, this is followed by generalized fasciculations and weakness which, in the most severe instances, may involve the muscles of respiration. The central nervous system effects include giddiness, restlessness, tremulousness, anxiety, headache, insomnia, and excessive dreaming. Changes in the electroencephalogram indicative of increased electrical activity of the brain have been observed. If the exposure is marked, ataxia, tremor, drowsiness, difficulty in concentrating, mental confusion, and occasionally disorientation develop. Paresthesias are common after exposure to TEPP, and changes in speech may occur after parathion. In the most severe instances, this is followed by coma with Cheyne-Stokes respiration and the disappearance of all reflexes, and then by generalized convulsions. Death has occurred in coma in from one to 13 hours after the onset of symptoms. The precise cause of death is not known, but contributing factors are believed to be depression of the respiratory and circulatory centers in the medulla, weakness of the muscles of respiration, and pulmonary edema.

The acute effects of the organic phosphate antiChE compounds last for from 6 to 30 hours, but mild symptoms may persist for several days. Occasionally the pupils may not return to the normal size for several weeks, probably because the antiChE compound has been sprayed or rubbed into the eyes. The only significant laboratory finding is the depression of the ChE enzymes of the blood and tissues; the only postmortem findings are hyperemia and edema of the lungs, and sometimes of the brain and other organs. Following death caused by parathion, the ChE activity of the plasma and red blood cells has been found to be reduced to 14 and 22 percent of normal, and that of the various tissues to between 22 and 88 percent of normal.

The effects of the antiChE compounds are attributable to inhibition of the ChE enzymes of the nervous system, muscle, and secretory glands, and not to the coincident inhibition of the ChE enzymes of the plasma and red blood cells. However, because it is not possible to determine the ChE activity of the tissues in man during life, it is necessary to rely on the ChE activity of the plasma and red blood cells as a guide of some value in detecting absorption of the antiChE compounds and the persistence of their effects. The ChE enzyme of the plasma is more sensitive to inhibition by the antiChE compounds now in use than are the enzymes of the red blood cells, brain, or muscle. The ChE activity of the red blood cells can be used as a rough guide to the activity of the tissue enzymes, but only if the exposure to the antiChE compound is relatively brief. If the exposure occurs over a longer period of time, this guide is less reliable, because the rate of restoration of the ChE activity of the red blood cells appears to be slower than that of the tissues in man.

The rate of restoration of the ChE enzymes following their depression by any of the antiChE compounds depends upon the reversibility of the ChE-antiChE combination, and upon the rate of regeneration of new enzyme protein. The combination between DFP and ChE enzymes is reversible for several minutes, following which the enzymes are permanently inactivated and their activity restored at rates which are compatible with the regeneration of new enzyme protein. The rate of restoration of plasma ChE (apparently by the liver) is approximately 14 percent of original activity on the first day, 9 percent on the second day, and from 2 to 6 percent on subsequent days until the activity has been restored to normal. The red blood cell ChE is restored at a uniform rate of approximately 1 percent of original activity per day, which probably represents the replacement rate of the red blood cells.

The combination between TEPP or parathion and ChE enzymes is partly reversible for several hours, following which the enzymes are permanently inactivated. During the first day after exposure to these compounds, the rate of restoration of the ChE enzymes of the plasma and red blood cells is more rapid, by about 10 percent of the original activity, than is the rate of restoration following exposure to DFP. After the second or third day, however, these enzymes are restored at the same rate as following DFP.

The exact rate of restoration of the ChE enzymes of the tissues following their depression by the antiChE compounds is not known in man. This restoration appears to occur over a period of many days, and to be slower after DFP than after TEPP or parathion absorption. For several days after exposure to any of these compounds, during which time the ChE enzymes of the tissues have probably not yet been restored to normal, there is increased susceptibility to any repeated exposure, and cumulative effects may occur. This cumulative action is particularly dangerous because there is a fairly narrow margin between the doses of these compounds that produce symptoms and the doses that are lethal, so that little or no warning may be given of impending serious effects. The oral dose of DFP or TEPP required to produce moderate symptoms is approximately 25 mg.; the lethal oral dose of these compounds is estimated to be about 100 mg. The comparable toxicity of parathion and DFP for experimental animals suggests that the dose-effect relationship of parathion for man may approximate that of DFP. It is probable that the ChE activity of the tissues may be considerably reduced by these compounds without the appearance of any warning symptoms; a further reduction below the level compatible with normal function may result in marked symptoms and even death.

The dangers of the organic phosphate antiChE compounds necessitate stringent precautions in their use, particularly in the case of insecticide preparations of parathion. These precautions include adequate warning labels, distribution only to properly instructed personnel, protective clothing (including gloves, goggles, and respirator), exhaust ventilation where possible, protection against wind dispersal, and careful disposal of contaminated material. Fruit, vegetables, or tobacco should be sprayed only with very dilute solutions, harvested not less than several weeks after the last spraying, and thoroughly washed prior to use. It is recommended that personnel who are exposed frequently have periodic determinations of the ChE activity of the plasma and red blood cells, and that those who develop reduction in ChE activity be removed from all exposure until this has been restored to normal, which will usually require several weeks.

Personnel contaminated with any of the organic phosphate antiChE compounds should have their clothes removed immediately and the skin washed. Atropine may be administered prophylactically. The treatment for symptoms attributable to the antiChE compounds is based chiefly on atropine, which has a moderate inhibitory effect on the muscarine-like, and a less striking effect on the central nervous system manifestations. Patients who have moderately severe symptoms caused by the antiChE compounds have an increased tolerance for atropine, so that fairly large doses may be given. It is recommended that 2 mg. of atropine be administered intramuscularly, at hourly intervals, or more often if necessary, until signs of atropinization appear. Following this, the dose of atropine may be reduced, but its administration should be continued as long as any signs or symptoms of the antiChE compound are present. Adjuvants to

atropine therapy include gastric lavage to remove any unabsorbed antiChE agent, parenteral replacement of fluids, and the administration of oxygen if needed. The occurrence of weakness of the pharyngeal and respiratory muscles may necessitate tracheal intubation and artificial respiration. If the convulsions are severe, the careful administration of ether or a barbiturate for their amelioration may be of value. Morphine should not be administered, as its action may be potentiated by antiChE compounds.

The organic phosphate antiChE compounds, which were developed for the most part as a result of wartime research, have proved to be useful in several ways, especially as insecticides. Newer and more potent analogues are being continually developed. It is hoped that appreciation of the properties and hazards of these compounds will prevent the harmful results of their careless or indiscriminate use. (Editorial, Ann. Int. Med., June '50, D. Grob)

Note: The organic phosphate insecticides will not be used by the Navy Department because of the extreme hazard of human poisoning. (Preventive Medicine Div., BuMed)

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Evaluation of Reading Efficiency of Marine Corps Personnel: One of the most prevalent forms of communication in the U. S. Marine Corps is the printed page. Many job duties require a tremendous amount of reading, such as of letters, manuals, bulletins, and regulations. Because military necessity demands an unequivocal understanding of these materials, it is essential that personnel be able to comprehend the content of such printed matter. The predominance of enlisted personnel in every unit indicates that unit efficiency often depends upon the ability of these men to interpret and retain the content of written material. Lack of such ability can seriously handicap individuals and greatly reduce unit effectiveness.

Absorption of content of written material is dependent, primarily, upon the relationship that exists between the reading ability of the men and the difficulty of the material read. Insuring content absorption for enlisted personnel requires both the evaluation of the reading ability of enlisted personnel and the use of this evaluation as a guide in the preparation of written material. To meet the first of these objectives, this study was designed to determine the average grade level at which Marine Corps enlisted personnel read, and to obtain the range of individual differences. The grade placement levels which were obtained in the study can then be used as reference points in the preparation of written material to be disseminated to a wide range of U. S. Marine Corps enlisted personnel. Individuals responsible for the preparation of written material should consider the reading abilities of those for whom the material is intended. If sentences are too complex, concepts are too abstract, and vocabulary too difficult for comprehension, many of the personnel will be unable to understand the content, and meaning will not be communicated.

The Progressive Reading Test and the Michigan Speed of Reading Test were administered to 522 white U. S. Marine Corps enlisted personnel of the Second Marine Division, Camp Lejeune, North Carolina. The means obtained were found to be highly similar to the median values; the medians are reported.

It was found that: the median grade placement of the sample on the Progressive Reading Test is at the tenth grade level; the median grade placement of the sample on the Michigan Speed of Reading Test is at the eighth grade level.

Moderately high intercorrelations (from 0.61 to 0.78) were obtained between vocabulary scores, comprehension scores, speed of reading scores, and General Classification Test scores. The first two measures are the subtests which comprise the Progressive Reading Test. The general trend of the data indicates that reading ability, as measured by this battery of tests, is related to the factors of education, age, and months of service. (Proj. NM 005 052.09.01, 19 April '50, Naval Medical Field Research Lab., Camp Lejeune, N. C., J. E. Rudasics)

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Medical Residency Training Program: Requests for residency training are now considered semiannually by the Bureau of Medicine and Surgery's Advisory Board on Postgraduate Education. The Board will meet during the first week of October and the first week of April and requests should reach BuMed sufficiently in advance of those dates to insure adequate processing before presentation to the Board.

Eligibility to compete for residency training in the Navy program is limited to medical officers of the regular Navy with selection criteria as indicated in BuPers Circular Letter 49-50 of 7 April 1950 (Medical News Letter, Vol. 15, No. 10, of 19 May 1950). In general, the number of requests for residency training in relation to available billets precludes selection of medical officers with less than one (1) year of active duty following internship. Requests for training must contain the required obligated service agreement as outlined in BuPers Circular Letter 49-50.

Although the Graduate Training Program for medical officers has been curtailed somewhat because of budgetary limitations and approaching fulfillment of the Navy's requirements in certain specialties, e.g., dermatology and syphilology, internal medicine, neurosurgery, obstetrics and gynecology, and general surgery, the program remains wide and varied, offering opportunity for the individual medical officer to acquire training in his chosen specialty. Currently, there are two hundred and fifty (250) training billets for medical officers in the naval hospital residency program and an additional fifty (50) billets for training in approved civilian institutions. It is the policy of the Bureau to assign first-year residents to naval hospitals in order to evaluate the individual medical officer's aptitude in the specialty before assignment to instruction at the second- and third-year levels. Priority for continuity of training is highest for those officers returning from a tour of sea or overseas duty.

As a matter of interest to medical officers who contemplate commencement or continuation of residency training and as a guide to the formulation of requests for such training, a listing of the approved residency training billets is presented herewith. Many of these billets are now filled but assignments to training, contingent on the Advisory Board's approval, may be made from time to time as vacancies occur.

RESIDENCIES IN NAVAL HOSPITALS

SPECIALTY	Bethesda	Chelsea	Great Lakes	Oakland	Philadelphia	Portsmouth, Va	St. Albans	San Diego	Total
Anesthesiology	2	2	0	2	2	0	2	0	10
Cardiology	1	0	0	0	0	0	0	0	1
Dermatology & Syphilology	0	0	0	0	3	0	2	3	8
General Practice	0	1	0	0	0	2	0	2	5
Internal Medicine	7	4	3	7	7	4	6	7	45
Neurosurgery	1	0	0	2	0	0	0	0	3
Obstetrics & Gynecology	6	3	3	6	3	4	3	6	34
Ophthalmology	2	0	0	2	3	0	2	2	11
Orthopedics	2	2	0	2	2	0	2	2	12
Otolaryngology	3	0	0	2	3	0	0	3	11
Pathology	4	0	0	2	2	0	2	3	13
Pediatrics	3	2	0	0	2	0	0	1	8
Psychiatry	7	0	0	0	5	0	0	0	12
Radiology	2	2	1	2	2	0	2	2	13
Surgery	8	4	3	8	9	6	7	8	53
Surgery (Plastic)	0	0	0	0	0	0	0	1	1
Surgery (Thoracic)	0	0	0	0	0	0	1	0	1
Urology	2	0	0	2	2	0	1	2	9
TOTAL	50	20	10	37	45	16	30	42	250

RESIDENCIES, FELLOWSHIPS, OR COURSES IN CIVILIAN INSTITUTIONS:

INSTITUTION	SPECIALTY	NO. TRAINING BILLETS
Alfred I. DuPont Institute Wilmington, Del.	Children's Orthopedics	1
Children's Hospital Boston, Mass.	Children's Orthopedics Pediatrics	1 1
Duke University Durham, N. C.	Children's Orthopedics	1
Harvard University Boston, Mass.	Public Health	1
Henry Ford Hospital Detroit, Mich.	Pathology	1
Illinois Eye & Ear Infirmary Chicago, Ill.	Ophthalmology	1
Institute of the Pa. Hospital Philadelphia, Pa.	Psychiatry	1
James Buchanan Brady Foundation of New York Hospital, New York, N. Y.	Urology	1
James W. Riley Memorial Hospital Indiana University Indianapolis, Ind.	Children's Orthopedics	1
Jefferson Hospital Philadelphia, Pa.	Psychiatry & Neurology	1
The Johns Hopkins University Baltimore, Md.	Public Health	1
Kings County Hospital Brooklyn, N. Y.	Neurosurgery	1
Lahey Clinic Boston, Mass.	Surgery	1
Langley Porter Clinic San Francisco, Calif.	Psychiatry	1
Boston City Hospital Boston, Mass.	Ophthalmology	1
Mayo Foundation Rochester, Minn.	Neurosurgery Radiology	1 1

Memorial Hospital New York, N. Y.	Oncology	1
Memphis Hospitals Memphis, Tenn.	Plastic Surgery	1
New England Deaconess Hospital Boston, Mass.	Pathology	1
New York Skin & Cancer Unit New York University, NYC	Dermatology & Syphilology	1
Northwestern University Chicago, Ill.	Surgery	1
Philadelphia Child Guidance Clinic Philadelphia, Pa.	Psychiatry	1
Shriners Hospital Honolulu, T. H.	Children's Orthopedics	1
Shriners Hospital Philadelphia, Pa.	Children's Orthopedics	1
St. Charles Hospital Brooklyn, N.Y.	Children's Orthopedics	1
Tulane University New Orleans, La.	Internal Medicine	1
University of Louisville Louisville, Ky.	Psychiatry	1
University of Michigan Ann Arbor, Mich.	Pathology Thoracic Surgery	1 1
University of Pennsylvania Philadelphia, Pa.	Anesthesiology Dermatology & Syphilology Internal Medicine Obstetrics & Gynecology Otolaryngology Pediatrics Surgery	1 2 4 2 1 1 5
Washington University St. Louis, Mo.	Otolaryngology Radiology	1 1
Wayne University Detroit, Mich.	Pathology	1
Total billets in civilian institutions		50

(Professional Div., BuMed)

Officers' Basic Course in Naval Medicine: The Bureau of Medicine and Surgery announces the re-establishment of a Basic Course in Naval Medicine beginning in September 1950 at the Naval Medical School, National Naval Medical Center, Bethesda, Maryland. The course is designed to prepare the naval medical officer in both clinical and naval medicine early in his career.

The curriculum embraces study of Medical Department duties, military and naval law, preventive medicine, medicine, surgery, neuropsychiatry, pathology, clinical biochemistry, hematology, serology, physical medicine, industrial hygiene and toxicology, physiology, and anatomy, with tumor conferences, clinical pathological conferences and library periods included. These studies are supplemented by 17 weeks of practical experience in naval medicine.

The following schedule has been planned:

SUBJECTS	DURATION	PLACE AND TIME
Reporting in		U. S. Naval Medical School week of 4 September
Amphibious Medical Training	2 weeks	Little Creek, Va. 11 Sep - 23 Sep
Medical Aspects of Special Weapons	1 week	Naval Medical School 25 Sep - 30 Sep
Submarine Medicine	2 weeks	New London, Conn. 2 Oct - 14 Oct
ABC Warfare	2 weeks	Edgewood Arsenal, Md. 16 Oct - 28 Oct
Field Medicine (Marines)	2 weeks	Quantico, Va. 30 Oct - 11 Nov
Aviation Medicine	2 weeks	Pensacola, Fla. 13 Nov - 25 Nov
Medical Logistics and Field Trip (Annapolis)	1 week	Naval Medical School 27 Nov - 2 Dec
Instruction in Professional and Military Subjects	3 weeks	Naval Medical School 4 Dec - 22 Dec
Period open for Christmas leave	10 days	22 Dec - 2 Jan

SUBJECTS	DURATION	PLACE AND TIME
Instruction in Professional and Military Subjects	9 weeks	Naval Medical School 2 Jan - 3 Mar
Fleet Exercises	5 weeks	Atlantic Fleet 6 Mar - 6 Apr
Instruction in Professional and Military Subjects	4 weeks	Naval Medical School 9 Apr - 3 May
Graduation Exercises		Naval Medical School 4 May

Requests for assignment to this course should be submitted to the Chief of the Bureau of Medicine and Surgery.

Assignment to this course represents permanent change of duty orders and will thus provide for the movement of dependents and household effects. (Professional Div., BuMed)

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Allergy-Arthritis Residency Available: One one-year residency in allergy-arthritis at the University of Virginia Hospital, Charlottesville, Va. is available now to medical officers of the regular Navy. In this training, residents see private patients under a tutorial system in the office and in the hospital. They work in the allergy and arthritis clinics, and serve as consultants for allergy patients on the medical wards. Each resident is required to take part in some form of investigation. Residents who have bachelor's degrees and two years of foreign language, ancient or modern, may register in the Graduate School, and a master's degree is conferred on those who pass a satisfactory examination and write an acceptable thesis. Requests for this residency should be forwarded to BuMed immediately. Dispatch requests should be confirmed by letter containing the service agreement. (Professional Div., BuMed)

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SECNAV LETTER Op24/clb, Serial 270P24 22 May 1950

To: All Ships and Stations

Subj: Disestablishment of U. S. Naval Hospital, Long Beach, Calif.

1. The following activity is disestablished effective 1 June 1950:

U. S. Naval Hospital
7th and Bellflower Street
Long Beach 4, California 3435-412

2. Holders of Basic Naval Establishment Plan, Fiscal Year 1950, after entering Change No. 1, delete paragraphs 7206 and 7206a.

3. Bureaus and offices concerned take necessary action.

--SecNav. Francis P. Matthews

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BUMED CIRCULAR LETTER 50-58 9 June 1950

From: Chief, Bureau of Medicine and Surgery
To: All Naval Hospitals

Subj: Ration Record, NavMed-36; Instructions Regarding the Preparation and Submission of

Refs: (a) BuMed C/L 44-91
(b) BuMed C/L 45-182
(c) BuMed C/L 46-84
(d) BuMed C/L 46-175
(e) BuMed C/L 47-80
(f) BuMed C/L 49-53
(g) BuMed C/L 49-74
(h) BuMed C/L 49-77
(i) BuMed C/L 47-135
(j) BuMed C/L 47-173
(k) BuMed C/L 49-168

This letter cancels references (a) through (h), paragraph 3 only of reference (i), and paragraph 5 only of reference (j). The primary purpose of the Ration Record is to show the number of subsistence days involved for all classifications of personnel authorized to receive or purchase rations, attached to the hospital. Secondarily, this report shows the total number of sick days applicable to the various classifications of patients and the total number of muster days applicable to military and civilian personnel attached. The Ration Record is to be submitted monthly together with the required monthly detailed reports of hospitalization (DD Forms 7), to reach the Bureau not later than the 10th working day

of the following month. Instructions (about 12 pages) are given for the preparation of the Ration Record.

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BUMED CIRCULAR LETTER 50-59 12 June 1950

From: Chief, Bureau of Medicine and Surgery
To: Commanding Officers, U. S. Naval Hospitals

Subj: Weekly Report of Enlisted Hospital Corpsmen; Cancellation of

Ref: (a) Par. 5145, MMD, 1945

1. Subject report is no longer required. Reference (a) is hereby canceled.

C. A. Swanson

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BUMED CIRCULAR LETTER 50-60 13 June 1950

From: Chief, Bureau of Medicine and Surgery
To: All Stations Continental having a Representative of the Medical Department

Subj: Report on Food Handlers Training Program

Ref: (a) BuMed CircLtr 50-13 (Not to all and not needed)

Encl: (1) Suggested Form for Reporting Training of Food Handlers

This letter (1) requests that the initial report (concerning food handler training courses) referred to in paragraph 6 of reference (a) be separate from but attached to the 30 June 1950 Sanitary Report, (2) gives instructions concerning information to be furnished on the report form enclosed, and (3) states that this circular letter is canceled after addressees have submitted the information requested.

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BUMED CIRCULAR LETTER 50-61 13 June 1950

From: Chief, Bureau of Medicine and Surgery
To: All Naval Hospitals and Medical Centers

Subj: Use of Metal Seals to Secure Patients' Gear

Ref: (a) Par. 516.2, MMD, 1945 edition

This letter states that reference (a) is modified to eliminate inventories of patients' personal effects when locks or serially numbered metal seals are used to secure patients' gear. Instructions concerning the disposition of such gear by the hospital, and its withdrawal by patients, are given. Comments and recommendations upon use of the subject seals should be referred to BuMed. An appropriate change will be made in reference (a) in the forthcoming reports chapter for the 1949 Manual of the Medical Department.

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BUMED CIRCULAR LETTER 50-62 16 June 1950

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Nonnaval Professional Examinations of Medical Officers; Request for Information Concerning

1. In order that the personnel records maintained in the Bureau of Medicine and Surgery concerning medical officers may contain all information required for orderly personnel planning, it is necessary that this Bureau be kept informed of any professional examinations, other than examinations for promotion, in which an officer intends to participate. Specifically, this includes examinations by specialty boards or state or national boards of medical examiners and which require that the candidates be assembled at a given time and place.

2. It is the responsibility of each such officer to notify promptly this Bureau concerning impending examinations of this type. This notification should be in the form of an official letter forwarded via official channels to the Chief of the Bureau of Medicine and Surgery, giving exact information regarding the title of the examining body, the nature and purpose of the examination, and the place and date on which it will be given.

3. Every effort will be made contingent upon the needs of the service to retain officers at stations for reasonable periods of time in order that they may participate in the above examinations. The highest priority for retention will be given for specialty board examinations. C. A. Swanson

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BUMED CIRCULAR LETTER 50-63 Joint Letter 26 June 1950

From: Chief of Naval Personnel
Chief, Bureau of Medicine and Surgery
Commandant of the Marine Corps
To: All Ships and Stations

Subj: National Service Life Insurance: Errors and Omissions on Applications and Related Papers

This letter, a copy of which appears in full in the 30 June 1950 Navy Department Bulletin states that the Veterans Administration has advised that applications for National Service Life Insurance and related papers are being received in that agency improperly executed and that errors and especially omissions in these applications not only cause delay in processing, but very seriously jeopardize the interests of the applicants and their beneficiaries. Addressees are requested to bring the contents of this letter to all personnel chargeable in any way with the processing of insurance matters to the end that better preparation of the documents incident to the granting and servicing of National Service Life Insurance will result.

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BUMED CIRCULAR LETTER 50-64 Joint Letter 27 June 1950

From: Chief of Naval Personnel
Chief, Bureau of Supplies and Accounts
Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Verification of Pay Records, Health Records, and Service Records

Refs: (a) Art. B-2304, BuPers Manual
(b) Para. 54602-1c, BuSandA Manual

This letter, a copy of which appears in full in the 30 June 1950 Navy Department Bulletin, broadens the scope of the verification required by reference (a) to include reconciliation, annually, of the service records with pay records and health records of all officer and enlisted personnel by a board convened by the commanding officer as of 1 September of each year. Instructions are contained concerning the board, the items to be verified, the procedures for verifying such items and remedying any discrepancies discovered, and the notations that are to be made on the records verified to indicate accomplishment.

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BUMED CIRCULAR LETTER 50-65 30 June 1950

From: Chief, Bureau of Medicine and Surgery
To: Distribution List

Subj: Hospitalization Rates for Fiscal Year 1951

Refs: (a) ALNAV 58-50
(b) Paragraph 53225.2 BuSandA Manual

This letter, addressed to all naval hospitals and certain naval stations within and without the continental limits of the U. S., states (1) that during the fiscal year 1951, the per diem rates to be charged and collected locally for in-patient medical care furnished certain supernumerary patients hospitalized in naval Medical Department activities are as follows:

Classification	Per diem rate
CIVILIANS, HUMANITARIAN, NONINDIGENT	
Continental activities	$11.25
Extracontinental activities	5.00
DEPENDENTS OF MILITARY PERSONNEL	1.75

(2) that during the fiscal year 1951, the value of the hospital ration as established by reference (a) is $1.0[illegible] and gives instructions concerning the accounting procedures.

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BUMED CIRCULAR LETTER 50-6 30 June 1950

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: BuMed Circular Letters

Ref: (a) Navy Department Bulletin Cumulative Edition of 1948, NAVEXOS P-632

1. BuMed circular letters issued prior to 1 January 1949 which appeared previously in compilations and semimonthly issues of the Navy Department Bulletin have been omitted from reference (a). This omission was made to avoid duplicating letters already appearing in the Bulletin of Bureau of Medicine and Surgery Circular Letters. An exception has been made in the case of letters issued jointly with other bureaus.

2. The Bulletin of Bureau of Medicine and Surgery Circular Letters is a cumulative loose-leaf compilation of all BuMed circular letters in effect. All officers of the Medical Department on active duty are required to possess and maintain in a current status a personal copy of the Bulletin of Bureau of Medicine and Surgery Circular Letters and the Manual of the Medical Department. These two publications, which are issued as a set, are furnished without request to such

officers upon entry into service. Ship and station office copies of these publications are available to activities having a representative of the Medical Department aboard. All requests for an correspondence regarding office and personal copies should be addressed to the Bureau. A. H. Dearing

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BUMED CIRCULAR LETTER 50-67 30 June 1950

From: Chief, Bureau of Medicine and Surgery
To: All Naval Hospitals

Subj: Collection Agents

Refs: (a) BuMed C/L 49-54
(b) Pars. 17000, 17004.6, 17220, 17221 BUSANDA Manual
(c) Par. 56035 BUSANDA Manual
(d) Par. 57039 BUSANDA Manual
(e) Par. 54102.4 BUSANDA Manual
(f) Par. 53225.1 BUSANDA Manual

This letter (1) cancels reference (a), (2) states that collection agents are assigned to duty at U. S. naval hospitals on the staff of the administrative officer in connection with the collection of monies for:

a. Hospitalization of dependents of military personnel, and of civilians, humanitarian, nonindigent.
b. Out-patient treatments and examinations furnished authorized civilian personnel (extracontinental hospitals only).
c. Miscellaneous services furnished by U. S. naval hospitals.
d. Subsistence furnished certain hospitalized inactive personnel, disability review cases and ex-service maternity cases.
e. Rations sold to authorized civilian personnel.
f. Rations sold to authorized military personnel and their guests.

(3) states that reference (c) outlines the general instructions for collection agents, and (4) gives information concerning collection of the monies involved, the accounting procedure, etc.

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